PEDIATRIC CLINICS OF NORTH AMERICA

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SYMPOSIUM ON NEUROPEDIATRICS

FOREWORD

M. A. PERLSTEIN, M.D.

Consulting Editor

This issue of the *Pediatric Clinics of North America* does not attempt to cover the field of Neuropediatrics, a subject which would take much more space and a much more astute editor to compile. It is rather intended to touch some of the high spots in the field of Neuropediatrics, particularly those newer aspects which reflect some of the recent developments in the field. It is thus hoped that it will fill a need somewhere between that supplied by textbooks which cover the subject in an encyclopedic manner and "year books" which give short reviews of the subject from a multitude of authors. In this volume the handling of each subject is more or less complete, although some of the items chosen are not necessarily representative of the most common problems in the field of Pediatric Neurology. An attempt has been made to handle the material at a clinical level. Much of the information which will be found here does not yet appear in the ordinary textbooks on the subject, and represents some of the newer aspects of Pediatric Neurology.

Some of the important, common everyday subjects covered herein include the technique of examination of the nervous system, bacterial infections and neoplasms of the central nervous system, convulsive disorders and neurosurgery in infants and children. Some of the more highly specialized items are treated in clinics on speech and hearing

difficulties, inborn errors of metabolism, the myopathies, the peripheral sensory disabilities and the late syndrome of posticteric encephalopathy. Some of the newer important, though esoteric, subjects are represented in the clinics on the development of postural and tonic changes in the newborn infant and on enzymology. Unique is a chapter on programs and resources available for handicapped children to aid the pediatrician who may have difficulty in knowing where to refer a handicapped child.

The editor is indebted to each of the experts who have contributed to this volume. It is hoped that some of the subjects not included in this volume will be covered in future numbers of the *Pediatric Clinics of North America.*

NEUROLOGIC EXAMINATION OF INFANTS AND CHILDREN

RICHMOND S. PAINE, M.D.

The principle of diagnosis of disease of the nervous system by examination of the function of its component parts is the same for patients of all ages. Obviously the method of examination and the interpretation of the responses, as well as the nature of the diseases to be looked for, will vary with age. Nevertheless, it is preferable to record the examination in much the same manner in all instances, although the length and importance of some sections will vary. There are several systems of writing up a neurologic examination; that given in Table 1 is one convenient plan. The purpose of such an outline is to encourage logical and orderly thought and to ensure against omissions. Misdiagnosis results more often from incomplete examination than from misinterpretation of findings.

MODIFICATION OF NEUROLOGIC EXAMINATION FOR INFANTS AND CHILDREN

Even those responses which can be tested in the conventional manner are often best observed in a sequence differing from that in Table 1. It is reasonable to begin with the most pleasant items and with those requiring the patient's cooperation or at least his nonresistance. Less important and more unpleasant tests are deferred until near the end. In infants and young children observation alone is the most important part of the examination, and may be the only way to appraise eye

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TABLE 1. *Recording of Neurologic Examination*

General appearance	
Mental state	Including apparent intelligence, personality and emotional factors
Speech (or any vocalizing)	Dysarthria
	Dysphasia
Tests for dyspraxia, body image concept disturbances, right-left confusion, etc.	
Head, neck and spine	
Special senses	Vision, including visual acuity, visual fields, eyegrounds
	Hearing
	Taste
	Smell
Cranial nerves	III, IV, VI
	V
	VII
	IX, X
	XI
	XII
Station and gait	Stair climbing and rising from floor
	Romberg test
	Automatisms of early infancy
	Postural maturation and responses
Motor function	Muscle power
	Muscle mass
	Muscle tone
	Coordination
	Tests of cerebellar function
	Involuntary movements

Reflexes:

	BJ	BR	TJ	Abdominal Upper	Abdominal Lower	Cremasteric	KJ	AJ	Clonus	Plantars
R.										
L.										

Sensation	Touch, pain, temperature
	Position, passive movement, vibration
	Stereognosis, 2-point discrimination, weight and size discrimination, figure writing perception (in palm of hand)
Autonomic	Lacrimation
	Salivation
	Skin color, temperature, triple response to scratch
	Perspiration
	Bowel and bladder function

movements, facial symmetry, coordination and gait. A valuable over-all impression is also obtained, and the experienced physician will often have reached a diagnosis from watching the baby while taking the history. The danger of snap diagnosis is great, however, and it is always desirable to evaluate the positive findings systematically.

It is not the purpose of an article such as this to describe the standard reflexes of adults, although most of them can be adapted for infants and children. The methods involved and their interpretation have been ably discussed by DeJong.[9] Many of these are not applicable to young infants, who furnish us, on the other hand, with a variety of automa-

Fig. 1. Special items useful in neurologic examination of infants and young children. Left to right: folding reflex hammer with small rubber tip suitable for very young infants (Solingen, Germany), reflex hammer with flexible handle (Allen and Hanbury, London), steel tape for measuring head and for testing grasp and visual fields, 4-inch red plastic ring on tape, pin wheel of type sold for Fourth of July, tracing wheel for sensory mapping (Singer Sewing Machine Co.), and collection of small common objects for testing for stereognosis and aphasia.

tisms and responses peculiar to this age period. Successful neurologic examination and diagnosis of infants depend greatly on an understanding of these. The field has been most conspicuously explored by Thomas[27] and Peiper.[23] Neither of these books is available in English, but Polani[24] has summarized Thomas's scheme of examination, and Dekaban[10] considers many points.

Little special equipment is required for the examination of infants, and it is possible to do a good job with only a reflex hammer, an ophthalmoscope, a safety pin and one's hands. A few other items which are often useful are shown in Figure 1.

One must bear in mind that a different type of lesion is usually

being sought from that to be considered with adults. Sharply localized vascular lesions, for example, are rarely encountered. The pediatrician deals more often with the gradual manifestation of congenital cerebral lesions or with relatively global progressive brain diseases. After acute illnesses the potential for recovery is, in general, greater than in adults, but there is also the need for a child to catch up with the progress of his agemates. Finally, the likelihood of neurologic symptoms being due to disease outside the nervous system is perhaps greater in infants and children than in adults. Convulsions may be due to hypoglycemia or hypocalcemia. Diseases of the heart, lungs, kidneys, endocrine glands or gastrointestinal tract can lead to "failure to thrive," with psychomotor retardation which might be erroneously attributed to "cerebral dysgenesis."

NEUROLOGIC EXAMINATION OF INFANTS

Observation

The examination should begin with observation of the baby's activities in bed, on his mother's lap or on the floor, without touching him and preferably from a sufficient distance not to upset him, although close enough for good vision.

Face. The faces themselves may show diagnostic stigmata of mongolism, cretinism, gargoylism, infantile hypercalcemia, and so forth. It is important to gain an impression of the baby's alertness, responsiveness, interest in his surroundings, relation to parents and to other people, and of such emotions as anxiety, irritability, apathy or remoteness. Responses to visual and auditory stimuli must usually be appraised chiefly in terms of facial expression, and this can usually best be done in a social way. Motor cranial nerve paralyses are most readily detected at this same stage of observation. An acute facial nerve paralysis is unmistakable, but a partial or recovering one may be puzzling (Fig. 2). Recovery, particularly in cases due to pressure at birth, usually occurs in the upper portion of the face first, so that at one stage the clinical picture might seem to resemble a supranuclear weakness. At a late stage contractures may make the paralysis appear to be on the opposite side. Inequality of the palpebral fissures may be the most obvious sign in some instances. The fissure is wider on the paralyzed side because of weakness of the orbicularis oculi; this may help in correctly lateralizing a doubtful case. Failure of development of the depressor of the angle of the mouth may cause asymmetrical crying with depression of the intact side and its absence on the affected side, a permanent disability.

Eyes. Having looked at the palpebral fissures, one should inspect the lids for possible ptosis. Only slight ptosis results from sympathetic paral-

ysis, but that from third nerve lesions is severe. Ptosis plus automatic elevation in rhythm with jaw movements is the Marcus Gunn phenomenon, a harmless congenital anomaly. The position of the eyes at rest should be noted. An especially important abnormality here is the setting sun sign[33] (Fig. 3), in which the irides appear to set beneath the lower lid. Sometimes this can be brought out by suddenly lowering the baby from a semi-sitting to a recumbent position. It occurs in mild degree in many normal prematures and in a small number of normal full-term infants, but if striking is suggestive of intracranial pressure or of brain stem irritation. It is a constant finding in kernicterus. The eyes are also

Fig. 2. Peripheral facial nerve paralysis. *A*, Right peripheral facial nerve paralysis present at birth. This is usually due to pressure against forceps or against the mother's pelvis. It is not obvious when the face is at rest, and only slight sagging of the right corner of the mouth can be seen in this instance. *B*, Paralysis obvious in crying. Note that the right eye cannot be closed. Ordinarily the palpebral fissures are wider on the paralyzed side at rest, although *A* shows the reverse situation. Width of the palpebral fissures in the neonate is often obscured by edema of the lids produced by silver nitrate drops.

to be observed for spontaneous movement and for possible nystagmus. Disconjugate movements may occur in normal newborns, but a great degree of roving movement later on suggests defective vision. Even newborns will often follow a red ring 4 inches in diameter, but ability to follow a moving light is not to be expected until 4 to 8 weeks. Interest in objects and response to faces are probably the first evidence of cortical activity and are important in the evaluation of babies after six weeks of age.

The size of the pupils is important, although congenital anisocoria is without significance. Dilatation of one or both pupils with absent constriction to light is one of relatively few neurologic signs requiring

diagnostic and therapeutic action in the newborn period. It usually results from pressure on the midbrain, most often as a complication of increased intracranial pressure. The irides of all white babies are blue at birth, but pigmentation occurs rapidly in those to be dark-eyed. Inequality of pigmentation may be the first clue to a Horner syndrome: the eye will remain blue on the side of the sympathetic paralysis, which might escape detection if it is difficult to hold both eyes open simultaneously.

MOUTH AND TONGUE. An enlarged and protruding tongue may represent simple macroglossia or may suggest mongolism or cretinism. Tremor of the tongue is without significance, but nonsynchronous fasciculations

Fig. 3. Setting sun sign of irides in early hydrocephalus.

of individual motor units are an important sign of active bulbar palsy, most often infantile spinal progressive muscular atrophy (Werdnig-Hoffmann disease or amyotonia congenita—see also p. 713). Fasciculations are difficult to see elsewhere in babies because of subcutaneous fat. Ceaseless, purposeless sucking movements of the mouth and tongue are suggestive of congenital defect of the brain or of a severe decerebration. The tongue deviates toward the paralyzed side in hypoglossal palsy. Babies of a year or more will sometimes stick out their tongues in imitation of the examiner. Below this age unilateral palsy is difficult to detect unless a lower motor neuron lesion is longstanding enough to produce hemiatrophy. A useful trick is to pinch the baby's nostrils; it will then open the mouth and usually elevate the tip of the tongue slightly. Infants in the first weeks of life normally show a retrusion reflex to expel objects placed on the anterior part of the tongue. If this is retained

past a month or two, it complicates efforts to give solid food and may be a sign of bulbar abnormality or future cerebral palsy.

Head and Neck. The size, shape and symmetry of the head should be considered for possible microcephaly, hydrocephaly or premature closure of cranial sutures. Bulging of the fontanel is another of the relatively few neonatal signs demanding prompt diagnostic action. Pulsation of the fontanel is normal and in fact argues against intracranial pressure. One should routinely listen for a bruit, although the majority of the softer of these prove without significance.[11] Retraction of the head, with stiffness of the neck, is the major feature of opisthotonos and is usually based on meningeal irritation from hemorrhage or infection, or on brain stem irritation or decerebration. It may be obvious even with the infant on his back (Fig. 4) or, in slighter degree, is easiest seen if the baby is placed on its side. Greater resistance to rotation of the head

Fig. 4. Opisthotonos in kernicterus.

to one side than the other may be an early sign of hemiparesis,[27] but is more often due to torticollis or positional plagiocephaly.

Body Posture. Opisthotonos is one abnormal posture of the body as a whole. Another is the pithed frog position of the legs. It may reflect disinclination to move, as in the rare cases of scurvy or acrodynia, but more often represents paralysis. The commonest cause is infantile spinal muscular atrophy, in which it is accompanied by universal hypotonia, areflexia, and paradoxical respirations with bulging of the abdomen and retraction of the chest (Fig. 5). Spinal cord injury appears superficially similar, but there is often abnormal posture of the arms in lower cervical lesions (Fig. 6).

The posture of the limbs at rest is also important. The asymmetry of brachial palsy is obvious. Hemiparesis, on the other hand, is rarely apparent in the newborn period unless due to a traumatic or anoxic insult at birth. In cases due to congenital cerebral lesions such as porencephaly, the earliest sign is usually poverty of movement of one arm and a greater tendency to keep that hand clenched than its opposite

(Fig. 7). Future bilateral cerebral palsy is suggested by continuous clenching of both fists past four months of age. In the legs the most sensitive suggestion of pyramidal tract abnormality or future spastic hemiparesis is a greater tendency to external rotation at the hip (Fig. 8). Pediatricians need not be reminded that congenital dislocation of the hip is a possible cause of delay in walking, and the gluteal folds, abduction range and other classic signs should be checked.

Fig. 5.

Fig. 6.

Fig. 5. Pithed frog posture with abdominal breathing and intercostal retraction, in infantile spinal progressive muscular atrophy (Werdnig-Hoffmann disease).

Fig. 6. Birth injury of spinal cord at C 7. The pithed frog posture of the legs resembles spinal muscular atrophy, but the abnormal position of the arms is a clue to a local cord lesion.

Spontaneous Movements. The normal movements of newborns are jerky and usually alternate in the case of the legs, but more symmetrical in the arms. They may be jittery or tremulous. Flexor postures of the limbs predominate. Premature infants, on the other hand, show greater tendency to extension of the limbs, and their spontaneous movements are often writhing and athetotic. Possible abnormalities include deviation from these qualities, asymmetry, or abnormal movements such as myoclonus or convulsions. Convulsions in infants under a month or two of age are usually clonic and of small amplitude and may escape notice. They are frequently focal or localized even in biochemical states such as tetany, but true jacksonian progression is probably not seen at this

age. Focal localized seizures are not necessarily a sign of cerebral cortical disease; they can occur in anencephalics.[31, 32] An exaggeration of the normal tremulousness of the newborn may be seen, in which the limbs show irregular clonic jerking of larger amplitude. This type of hyperkinesis is increased by stimulation and frequently follows anoxic birth.

Respirations. The nature, rate and rhythm of breathing are important clues to brain stem function. Abdominal breathing with intercostal retraction is a conspicuous sign in birth injuries of the spinal cord. In

Fig. 7.

Fig. 8.

Fig. 7. Right hemiparesis at age 2 months. There is little difference in tone and none in reflexes, but the abnormal posture of the right arm and the closed right hand are striking. Leg involvement becomes obvious only later in most cases, and a misdiagnosis of brachial palsy is sometimes made. Hemiparesis due to congenital lesions is seldom apparent under this age.

Fig. 8. Externally rotated position of left leg in recumbent position. A sensitive sign in hemiparesis or unilateral pyramidal tract lesions.

spinal muscular atrophies and in infantile muscular dystrophies the intercostals are usually weakened earlier than the diaphragm, so that the result is a respiratory pattern identical to that in cord injuries.

Hand Function. In addition to observing spontaneous movements, one should study hand function by offering a dangling object. The baby can be lying on its back or sitting in bed or on its mother's lap. Babies as young as three months will grasp at the object, but effective seizing of it on contact is more reliable at four to five months. A steel tape such as is used for measuring head circumference is one of the best test objects. The usual evolution of grasp is for the baby to approach

and take the object at 5 months, to take it by apposing the thumb to 2 or 3 fingers at 7 months, and to show thumb-to-forefinger grasp for small objects at 9 or 10 months. The last-mentioned is easiest seen as the baby picks up a small pill from a flat surface. Delay in this sequence may reflect inadequate mental development, poor vision or a motor

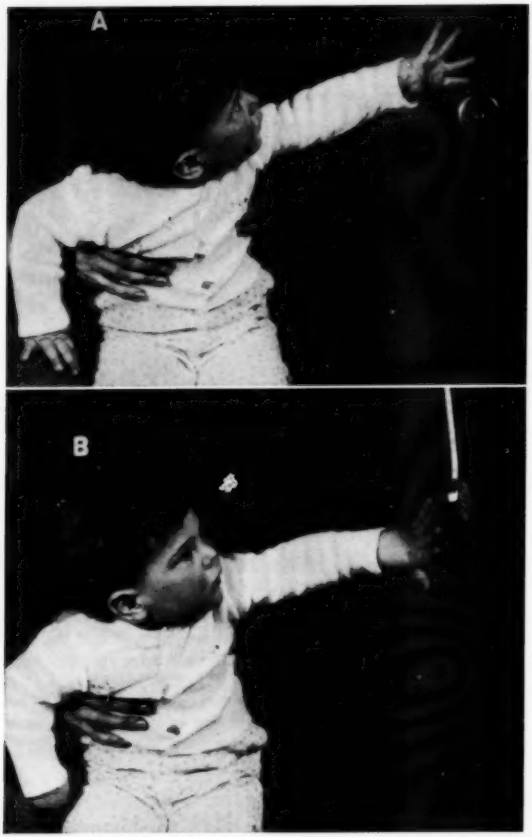

Fig. 9. Early athetosis in a child of one year, with avoiding reflex of hand.

disability, but one should ascertain by repeated trial that failure is constant. Athetosis becomes evident as a squirming instability between opposing postures and is suggested by an avoiding reflex in which the hand seems automatically withdrawn from the object as it touches it. Unmistakable athetosis is rare before 18 to 24 months, but suggestions of it are often recognizable earlier (Fig. 9), even down to 6 months.

Feeding Behavior. Inability to suck, chew or swallow may be important evidence of congenital brain defect in the first few months. The reports of experienced nurses are invaluable, but the physician should also observe for himself.

Stance and Gait. Stance and gait of older infants should be observed at this point in the examination, much as with older children.

Special Senses

Vision. Vision must largely be assessed indirectly. The pupillary reaction to light is retained in lesions of the optic radiation and cortex. Fixation on and following objects are the principal criteria of vision. Most newborns will on one occasion or another follow a 4-inch red ring, and optokinetic nystagmus can be obtained with the apparatus of Gorman and Gellis.[14] Reliable following of objects such as steel tape cases is more a matter of six to eight weeks, however, and the first evidence of vision may be the baby's response to its mother's smile. Greatly disconjugate or ceaseless roving eye movements suggest blindness. The convergence response is present by about three months, but miosis accompanies it only somewhat later.[27] A blink reflex can be obtained to a strong light in the newborn. The blink response to a menacing gesture of the hand is a useful test at two to four months, but the hand must not be moved rapidly enough to produce a breeze. However, in the great majority of instances apparent blindness at ages under four months will subsequently turn out to be the result of mental deficiency with more or less normal vision. Cortical blindness is rare in infancy except as a manifestation of occipital malformations (such as a large porencephaly, which might be shown by transillumination) or of degenerative diseases.

Hearing. Even newborn infants will startle, blink or execute a Moro response to loud noises. The response may be absent on some occasions, however, and repeated testing is necessary. A bell, a metal clicker, snapping or rustling of the fingers, and the human voice are the most useful tests for older babies. The criterion of hearing is chiefly turning of the eyes or head in the direction of the sound, which can be expected in some degree by three months of age. A change in the respiratory rate or pattern may be recordable earlier than this.[23] Finally, the mother's impression of whether or not the baby hears is to be taken seriously, since deafness is often suspected by parents or grandparents before its recognition by the physician. An excessive startle reaction to sound is an important clue to progressive cerebral degeneration, especially Tay-Sachs disease.

Smell and Taste. Smell and taste can be examined even in babies by offering strong odors or by placing sweet, salty or bitter substances

in the mouth and observing the facial expression, but the test is of little clinical value at this age and in any event should be deferred until later in the examination.

Tests Requiring Minimal Handling

TENDON REFLEXES; CLONUS; PLANTAR REFLEXES. These are tested in the conventional manner. The knee jerk and biceps jerk can be obtained from the newborn period on, but it may be difficult to get the baby sufficiently relaxed. The triceps and ankle jerks are usually unobtainable in the first month unless the normal flexor tone is for some reason reduced (as in prematures). The triceps jerk is easily obtained in the presence of an upper brachial palsy. The head should be kept in the midline while testing the knee jerk, since a tonic neck pattern may in-

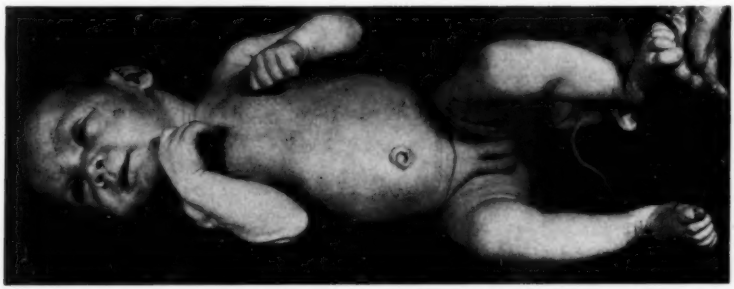

Fig. 10. Position for testing ankle clonus in a baby of 3 weeks. Ten or a dozen beats may be normal.

crease or diminish it. Overflow of the knee jerk to include adduction of both thighs is normal in the first six months.[3] In testing ankle clonus the entire leg should be free in the air and only light pressure exerted against the sole of the foot (Fig. 10). As many as a dozen beats is normal in the first few weeks of life. The plantar response is of no clinical value in infancy unless it is asymmetric or abnormally strong in degree. A "positive Babinski" is normal until one or two years of age and sometimes later. Its disappearance does not necessarily coincide with the ability to walk. The principal features of a pathologic response in infancy are the more extreme and sustained extension of the great toe and the greater degree of fanning of the other toes. A "positive Babinski"-like posture is also one phase of athetosis of the foot. The standard of normal for tendon reflexes varies greatly. A lively ankle jerk, even duplicated two or three times if there is coincidental extensor thrust by the patient, is normal in one child, while another may be almost, but not quite, areflexic. Slight hyporeflexia or hyperreflexia

means little unless it is asymmetric or changed from a previous examination.

Rooting and Sucking. The rooting response (*réaction des points cardinaux*) consists in the baby's following the examiner's finger to the right, left, upward or downward when the mouth is touched at the four points of the compass (Fig. 11). It may be absent if the baby has been recently fed, but can be reinforced in doubtful cases by testing the sucking reflex to the finger in the mouth previously. Rooting and sucking should be present in babies other than the smaller prematures, and their absence suggests chiefly depression of the central nervous system, as from anoxia or maternal anesthesia, or congenital defect. The rooting response persists until three or four months of age and as late as seven

Fig. 11. Rooting reflex (*réaction des points cardinaux*).

or eight months during sleep.[15] At the later ages visual cues play a part, and babies may root for a bottle when they will not for a finger. Both rooting and sucking may be uncovered by extreme decerebration in later childhood.

Movement of Head in Response to Touch. From the newborn period on, digital stimulation of the nostril or ear will usually produce motion of the head. This response may be absent in general depression or anomaly of the nervous system.

Palmar and Plantar Grasp. Palmar and plantar grasp are automatic reactions of full-term newborns and are elicited by placing the examiner's finger firmly in the palm or at the base of the toes. Both are strong. The palmar grasp response weakens as the hand becomes less continuously fisted at three or four months, and the plantar grasp by

about eight months. Possible abnormalities are failure to obtain these responses or their asymmetry.

ALLONGEMENT CROISÉE AND MAGNET REFLEX (RESPONSES TO PRESSURE ON THE FOOT). From the newborn period until four or five months of age, firm pressure against the sole of one foot will produce adduction of the opposite leg followed by its extension, the opposite foot coming down the stimulated leg as if to push the examiner's hand away (Fig. 12). This is a normal type of crossed extension usually designated, in French, *allongement croisée*, and distinct from the crossed extension response to pin prick, seen with spinal cord lesions. At a later age a magnet response may be obtained in which the stimulated leg tends to follow the examiner's hand as it is withdrawn.[1] The sole tends also to maintain its apposition to a flat surface, especially if the baby is upright.

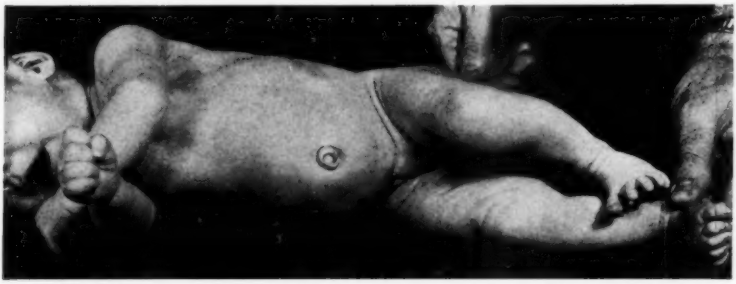

Fig. 12. Normal crossed extension reflex of young infants (*allongement croisée*). Pressure on the sole of the right foot results in flexion, adduction and then extension of the left leg along the right as if to push the examiner away. This is to be distinguished from the abnormal crossed extension response to pin prick seen in the presence of spinal cord lesions.

TRACTION RESPONSE. The traction response is tested with the infant on its back, it then being drawn up to the sitting position by the hands. Normally assistance by the shoulder muscles can be felt and seen. The newborn's head lags behind and flops forward suddenly when the upright posture is reached (Fig. 13). Even in the newborn period, however, there should be sufficient head control to bring it back upright, and greater control is expected with age. The response is asymmetric in brachial palsy or hemiparesis. It may be absent in hypotonic states, including spinal muscular atrophy, general nervous system depression, and also strikingly in mongolism.

"DOLL'S EYE" MOVEMENTS. In the young infant eye movements must be tested by vestibular and otolith stimulation. "Doll's eye" movements may be obtained from birth by moving the head sideways or up and down. These are another type of automatism which may re-emerge in

Fig. 13. Traction response. Baby has been drawn from the supine to the sitting posture. Its shoulder muscles "assist," and head control should be about of the degree shown (age 3 weeks).

severe decerebration at a later age. Rotational testing is more valuable, but should be deferred until slightly later.

Muscle Tone. During all the preceding maneuvers the examiner will gain an impression of the tone and range of motion of the neck, trunk and limbs. If this appears increased, decreased or asymmetric, further manipulation is appropriate.

Tests Requiring Greater Handling

Prone Posture. When placed on the abdomen, the normal newborn will turn the head to one side, possibly raise it slightly, and will usually make creeping movements with the legs. The arm may be brought forward on the side toward which the head turns. The normal response is variable from one time to another, but what is to be sought is some effort by the baby to extricate itself from the position in which he is placed (Fig. 14). Absence or persistent asymmetry of this is abnormal.

Eye Movements to Rotation. Eye movements to rotation are tested by picking the infant up and holding it opposite the examiner (Fig. 15), who then rotates about his own axis for several revolutions to the right and then to the left. The baby will look ahead in the direction of rotation on acceleration and after stopping will look back in the opposite direction.[19] This appears to be the reverse of the situation in a Barány chair. It is, however, physiologically the same because the baby is facing the axis of rotation at a distance rather than over it and because his turning with respect to his own axis is in effect in the opposite direction to that in which the examiner swings him. Abducens paralyses are immediately obvious in this maneuver. It is surprisingly undisturbing to the baby, who will in practically every instance obligingly open the eyes. Some infants show only forced deviation of the eyes, but nystag-

mus is usually present; interpretation of variation needs further investigation.

STEPPING; PLACING; POSITIVE SUPPORTING. Normal newborns, if awake and vigorous, will execute spontaneous stepping movements when the trunk is supported, inclined forward and slowly advanced. One foot

Fig. 14. Three-week-old baby in prone posture.

Fig. 15. Testing of extraocular movements by vestibular stimulation by rotation. (See text.)

must initially be brought firmly into contact with the table surface (Fig. 16). It is a response to foot pressure and trunk motion, and can also be obtained on a wall or even on the ceiling.[23] This automatic walking usually disappears by two to four weeks. Placing (Fig. 17) is a response which should be present from birth: the dorsum of the foot is brought up against the under surface of a table edge, after which the

child will lift its foot and place it squarely on the table.[26] Both stepping and placing vary from time to time and may be unobtainable in uncooperative or sleepy babies. They are missing in anencephalics and are sometimes stated to be cortical responses; more probably little if any neonatal activity is actually derived from the cerebral cortices. Asymmetry in placing, however, may be an early sign of hemiparesis. If the newborn is suspended upright and both feet are placed against a flat surface, the legs stiffen somewhat, but the knees do not extend and little weight is borne. This response is lost by a few weeks of age, and

Fig. 16.

Fig. 17.

Fig. 16. Automatic "walking" of the first few weeks of life.
Fig. 17. Placing response. Dorsum of left foot has just been brought up under table edge, and baby places it firmly on top.

the true positive supporting reaction[26] to bear weight is not consistent until about six months. It may appear earlier and stronger than normal in spastic diplegia.

Vertical and Horizontal Suspension. When infants of any age after two months are suspended vertically by the examiner's hands under the axillae, there should be sufficient neck control to maintain the head. The legs normally flex up to four months of age and move about after that age. Fixed extension of the legs, particularly if adducted or scissored, is one of the earliest signs of spastic paraplegia or diplegia (Fig. 18). If the baby is in the vertical position, pressure with the hand against the forehead or occiput will be resisted by the muscles of the neck.[27]

Fig. 18. One-year-old baby showing abnormal hypertonic extension and adduction of legs in vertical extension. This is an early sign of spastic diplegia.

Fig. 19. *Redressement du tronc.* Baby is suspended horizontally with buttocks against examiner's chest and legs hanging down. Pressure against feet produces elevation of trunk and head.

It is not until several months of age that suspension in the horizontal position (with the abdomen on the examiner's hand) will produce elevation of the head as if to look up. The legs should be flexed on the trunk in the newborn, however, and limp collapse into an inverted U is a sign of general hypotonia, as in mongolism. A trunk elevation response (*redressement du tronc*) can be obtained in vigorous newborns, or at least by two or three weeks of age. The baby is suspended horizontally, bent at the waist, with the buttocks against the examiner's chest.

Fig. 20. Landau reflex at 11 months. Depression of head in horizontal suspension is followed by flexion of legs. At a slightly later age the legs would have initially been hyperextended upward.

Firm pressure against the soles of both feet will then be followed by elevation of the trunk and head (Fig. 19).

In horizontal suspension older infants will raise the head to look up and extend the legs (or hyperextend upward after eight or nine months of age). At this stage the Landau response may be shown:[18] depression of the head by the examiner's hand will be followed by flexion of the legs on the trunk (Fig. 20). This persists until a year or two of age.

Trunk incurvation response is phylogenetically primitive and is obtainable even in the smallest prematures[2, 27] and in anencephalics.[27]

With the infant in horizontal suspension, the head and trunk inclined slightly upward (or in the prone position on a table), the examiner's finger is run down the paravertebral area. There is firm swinging of the pelvis toward the stimulated side (Fig. 21). The response may also be elicited by pinching the skin just above the pelvic brim on either side. Its absence indicates a spinal lesion or general depression or abnormality

Fig. 21. Trunk incurvation response to finger running down paravertebral area.

of the nervous system. It is, however, variable enough from time to time to require repeated examinations.

In suspension with the head and shoulders inclined downward, a normal baby of two or three weeks may extend the hands.[27] There is relatively little hyperextension of the neck, but this and a flinging out of the arms as if to check the fall will be seen when a baby past eight or nine months is suddenly projected toward a flat surface (the parachute response[23]) (Fig 22).

Tonic Neck and Neck Righting Reflexes. The tonic neck reflexes[20] have their origin in the proprioceptive endings in the neck muscles and

brain stem representation at the level of the red nucleus, in animals. If an infant is lying on its back and turns its head to one side or if the head is turned to one side by the examiner, a positive response consists in a degree of extension of the arm and leg toward which the face is turned with flexion of the opposite arm and leg. There is usually no constant pattern in newborns. The response is normally at its physiologic height between two and four months of age, when normal babies spend a considerable proportion of their day lying in these positions[13] (Fig. 23). The patterns can also be partially imposed on them by the examiner's rotation of the head, but the baby should be able to overcome the pattern by vigorous struggling; completely obligatory tonic neck patterns are pathologic at any age.[4] The responses normally dis-

Fig. 22. Parachute response in 11-month-old baby as it is plunged toward table top.

appear by six months of age. Delayed retention of a slight tonic neck reflex may occur in general psychomotor retardation. but retention in strong form is a major sign of motor postural disability.

This is one feature distinguishing the hypotonic helpless baby of 12 months with a future athetotic cerebral palsy from those with spinal muscular atrophy, spinal cord injury or infantile myopathy. One should, in fact, hesitate to ascribe failure to sit at this age to "cerebral palsy" if there are not clear tonic neck reflexes. The patterns may be retained into adult life, and in the cerebral palsies they are, if pronounced, generally incompatible with independent standing balance and should be considered in planning physical therapy or orthopedic surgery (Fig. 24). Tonic neck reflexes may reappear at any age in decerebrating states. They may also be retained or increase without ever having disappeared

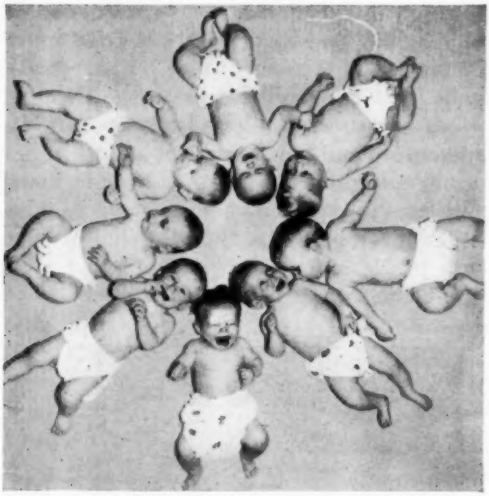

Fig. 23. Many of a group of normal 4- and 5-month-old babies tend to lie in partial tonic neck patterns. (Lloyd Nolan, Black Star.)

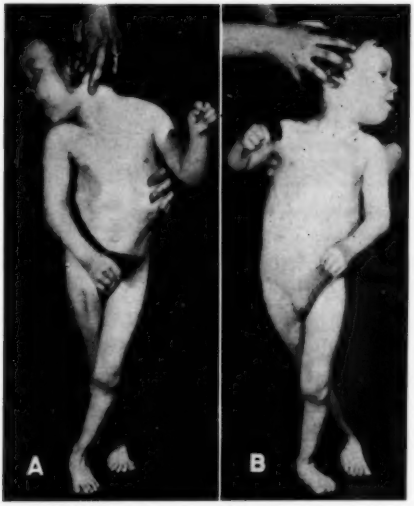

Fig. 24. Persistent obligatory tonic neck patterns in a 2-year-old with spastic diplegia. Note also scissoring of legs. This degree of tonic neck reflex is almost always incompatible with standing balance.

if the degenerative process begins at two to six months of age, as in Tay-Sachs disease.

As the tonic neck response is lost, it is replaced with a neck righting reflex in which passive or active rotation of the head to one side is fol-

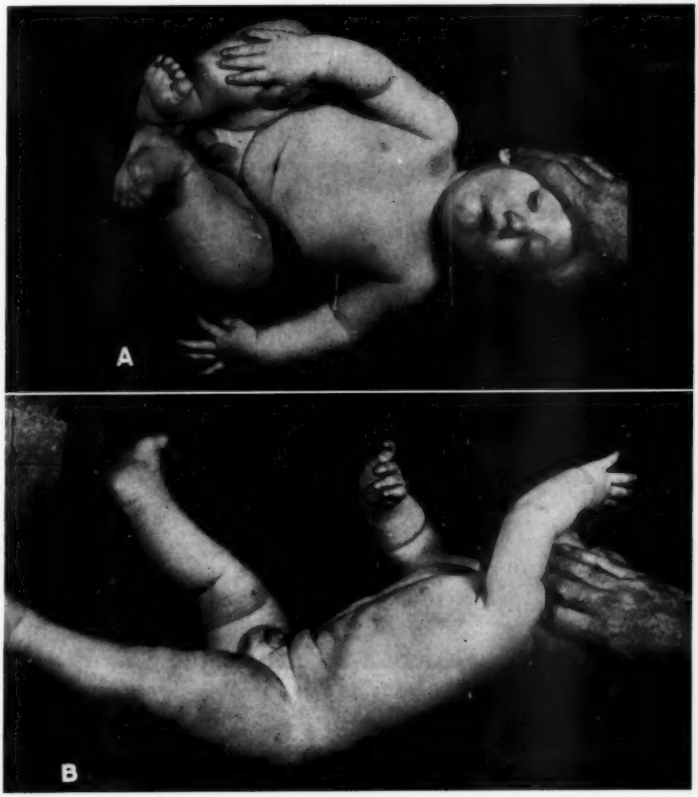

Fig. 25. Neck righting reflex. Rotation of head to right is followed by turning of shoulders, trunk and legs in same direction. In this instance the 9-month-old patient has a spastic diplegia and shows the neck righting reflex in an abnormally stereotyped obligatory degree. Less obligatory versions are normal, up to 2 or 3 years.

lowed by rotation of the shoulders, trunk and pelvis in the same direction (Fig. 25). This is probably a useful automatism in the process of rolling over, which at a later age is followed by rising from the floor in the quadripedal manner. Traces of the neck righting reflexes persist to one to two years of age, but obligatory, stereotyped reflexes are pathologic and often found in cerebral palsies.

MORO REFLEX. The reflex of Moro[22] consists in extension of the arms followed by their flexion with spreading of the fingers, and flexion of the femora on the pelvis in most instances. It is a response which can be set off by a variety of afferent pathways, including slapping one's hands on the mattress (Moro's original method), striking the bassinette, a loud noise, grasping the infant's hands and extending and then releasing them, or by picking up the head of the bassinette and suddenly dropping it. The most innocuous and reliable method, however, is to lift the shoulders and head slightly in the air, and then let the supported head extend about 30 degrees with respect to the trunk (Fig. 26).

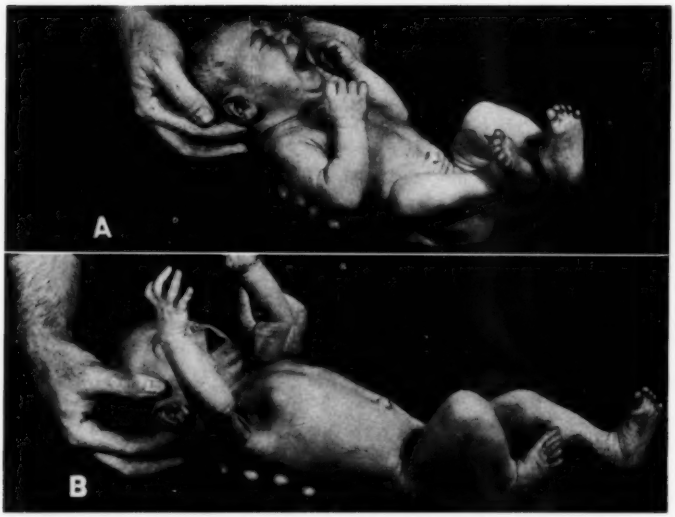

Fig. 26. Moro reflex. Head is allowed to drop back about 30 degrees with respect to the axis of the trunk.

The Moro response is missing or incomplete in the younger prematures, but should be regularly obtainable in any normal full-term baby. Its defect or absence can be due to a variety of causes, including severe systemic illness of any type, general depression of the central nervous system and, conspicuously, kernicterus. In fact, a defective Moro, opisthotonos and the setting sign of the eyes are the principal and probably indispensable physical signs of kernicterus in the first week of life. An asymmetric Moro is seen in the presence of brachial palsy or in the rare cases of neonatal hemiplegia. Fractures of the clavicle or humerus or injury to the shoulder joint are commoner causes of asymmetry. The Moro response begins to fade by four to eight weeks, at which stage it becomes incomplete and sometimes asymmetric. It can be reinforced by

pressure against the knees, and slight flexion of the femora on the pelvis in this maneuver is probably the last trace, even up to six months.[17] Prolonged retention of the Moro response is occasionally seen in cerebral palsy, but is less usual and of much less clinical value in this respect than is the tonic neck response.

SENSATION. Sensory thresholds for touch, pain and temperature are all higher in young infants than in older children, and reaction is relatively slow. Touch can often be appraised by tickling the baby's feet, hands or other parts of the body. Response may take the form of withdrawal, local movement, rippling of the skin or change in facial expression. More definitive sensory examination must be done with a pin, using the same criteria of response if possible. If pin prick must be firm

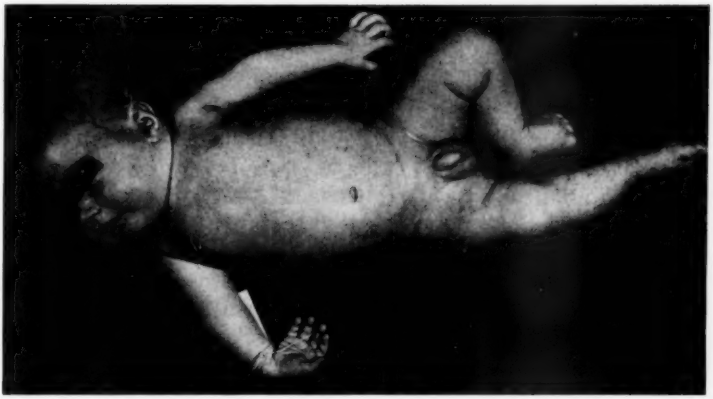

Fig. 27. Posture of baby with birth injury of spinal cord after pin prick to left foot. The left leg is withdrawn, followed shortly by vigorous extension of the right. Note also abnormal hand postures (lesion at C 8 and T 1).

enough to produce crying, it is usually impossible to test more than a small area at a time, and complete examination may take days. After preliminary sensory testing the withdrawal response of the foot to pin prick should be checked. Feeble pricking may produce extension, but stronger pricking should cause withdrawal of the stimulated limb and facial evidence of pain. Withdrawal may be lacking if there is either paralysis or anesthesia, but appreciation of pain is clear in such diseases as spinal muscular atrophy. Spinal cord lesions produce a characteristic crossed extension reflex. The pricked foot and usually the whole leg withdraw in an automatic and often clonic way, followed by vigorous extension of the opposite leg (Fig. 27). The face usually shows no evidence of feeling of pain. The upper level of anesthesia can be demonstrated by progression up the body with the pin. The tonic neck

reflexes help to distinguish extrapyramidal cerebral palsy from spinal muscular atrophy and spinal cord injury, but the differential diagnosis between the two last-mentioned rests principally on the response to pin prick.

EYEGROUNDS. The eyegrounds of infants of two to six months are usually easily examined, provided one makes the initial attempt with as little restraint as possible. Sometimes the fundi can be successfully seen while the baby is carried over its mother's shoulder, but it is usually preferable to have the child lying flat on its back in a darkened room. Under two months and after six, babies generally resist examination, and restraint of the head is practically always needed. Mydriatic drops are essential for complete examination, but a satisfactory screening inspection can often be carried out without them. Children above the age of two may be seated on a chair or table and their gaze attracted by a rotating pinwheel (Fig. 1). The sparks can be seen in the dark and will hold the child's gaze away from the ophthalmoscope light. The same device may be used with a baby lying on a table, which better fixes the head.

The normal optic disk is considerably paler in infancy than in later life, and a diagnosis of optic atrophy must be made with caution. Papilledema is infrequent while the fontanel is open even if intracranial pressure is increased. Congestion or tortuosity of the vessels, suppression of their normal pulsation, or the presence of hemorrhages are possible indications of intracranial hemorrhage or venous obstruction, although retinal hemorrhages are seen in many apparently normal newborns if they are carefully examined. Increased intracranial pressure is more likely to produce papilledema once the fontanel has closed, but up to three years (and occasionally later) the sutures may separate so rapidly as to relieve the pressure without papilledema's becoming evident.

TRANSILLUMINATION OF THE HEAD. The head of any baby suspected of neurologic abnormalities should be transilluminated. A strong flashlight is fitted with a rubber adapter to make a light-tight seal against the head. The baby is then taken into a totally dark room, and the examiner holds the flashlight against different areas of the head. There should be no transillumination from front to back or side to side. A small halo around the point of contact is normal on the anterior head, but is minimal on the occiput. Hydranencephaly may be recognized from total back to front transillumination of the head. Large porencephalic cysts or extensive hemispheric atrophy may show as local transilluminations. It may even be possible to ascertain that the abnormal fluid is loculated. Unilateral absence of the expected normal halo around the rubber adapter when the light is placed against the midforehead may suggest subdural hemorrhage on that side. (Effusions of clear fluid transilluminate, but fresh blood does not.)

Developmental Evaluation

Just as comment on the patient's mental state is always a part of the neurologic examination of an adult, some estimate of developmental adequacy is indispensable in examination of infants and children. Quantitative evaluations, particularly in such matters as adoption cases, are clearly tasks for qualified clinical psychologists. Nevertheless, the physician must decide from his own examination whether or not psychological referral is required. This, of necessity, involves the borrowing of certain criteria from the standard psychological tests with an under-

TABLE 2. *Clues for Appraisal of Development by Responses to Visual and Auditory Stimuli, and Sound Production*

AVERAGE NORMAL DEVELOPMENTAL LEVEL (MONTHS)	VISUAL RESPONSES	RESPONSES TO SOUND AND VOCALIZATION
0	Blinks to light Follows red ring at times	Responds to handclap or clacker
1	Looks at person momentarily	Responds to bell, click or rattle
2	Smiles at mother Follows moving object with eyes momentarily Recognizes mother Turns eyes toward fixed light	Momentarily turns eyes to side of sound
3	Looks at hands Turns head to follow moving object Reacts to paper on face	Distinguishable sounds in addition to cry Quieted by music or voice
4	Follows ball rolling across table	Turns head toward sound source Laughs
5	Looks at pellet	Cries when object taken from him
6	Approaches mirror	Vocalizes eagerness, pleasure, displeasure
7	Smiles at image in mirror	Babbles several distinguishable syllables
8	Plays peekaboo	
9	Looks at pictures Looks for fallen objects	Says "dada" or "mama" or other double syllable Responds to name and to "no-no"
10		Distinguishes a few spoken words
11	Looks for contents of box (presented first filled and then empty)	
12		Imitates spoken words
14		3–4 words (besides "mama" and "dada")
15		4–5 words, including names
16		Says spoken words spontaneously
18		Uses words to make wants known Names objects shown to him Vocabulary of about 10 words
21		Names objects in pictures
24		Says 2 or 3 word phrases

standing of their limitations, the range of normality, and the disadvantage at which the physician finds himself in using them. His regular office is not the most desirable setting, but many of the criteria have been used for years, consciously and subconsciously, by experienced pediatricians, who are often keen in their impressions.

Tables 2 and 3 outline some of the standards which can be used for testing or, within limit, by maternal description, allowing for optimistic overestimation. The ages given are averages, the variation of normal often several months, and failure to do an item does not have pathologic significance until an appreciably later age.[12] Only little and readily

TABLE 3. *Clues for Appraisal of Development by Motor Accomplishments*

AVERAGE NORMAL DEVELOPMENTAL LEVEL (MONTHS)	HAND FUNCTION (LATER ITEMS ARE ADAPTIVE BEHAVIOR)	POSTURE AND BALANCE
0	Fists clenched most of time Palmar grasp reflex present	Turns head to side in prone position and makes creeping movements of legs
1	Maintains grasp of object placed in hand	Lifts head from bed in prone position Lifts head from shoulder in vertical position
2		Holds head erect in vertical position "Swimming" movements of legs in bath
3	Hands open about half of time Manipulates objects	Turns from side to back Tenses body when about to be picked up
4	Plays with rattle Splashes with hands in bath Feels and grasps table edge Reaches for dangling object	Holds head steady when moved around in vertical position Pushes chest up with arms in prone position
5	Recovers rattle Picks up small block on contact Transfers objects hand to hand	Rolls over back to abdomen Sits supported when placed
6	Approaches and grasps cube Bangs with spoon or stick Lifts cup	Sits briefly unsupported if placed
7	Attempts to "scoop" up pellet Plays with string or paper Rotates wrist Holds a block in each hand at same time	
8	Opposes thumb and 1st 2 fingers to hold block Obtains ring by pulling attached string Lifts cup by handle	Sits securely unsupported on floor if placed
9	Midline bimanual play (patty cakes or bangs 2 objects together) Picks up small block with thumb and forefinger	Achieves sitting position unaided

TABLE 3 (*continued*)

	IMITATIVE BEHAVIOR DEPENDING ON VISUAL AND AUDITORY CUES, AND HAND FUNCTION	
10	Conditioned tricks such as patty cake, bye-bye, etc.	Stepping movements when held upright
	Puts object into cup, in imitation	
	Rings bell imitatively	
	Grasps small objects promptly	
	Lifts cup to uncover object	
11	Uncovers toy by removing cloth	Pulls self to standing position, holding on to furniture
12	Stirs with spoon in imitation	Sits down unassisted from standing position
	Holds cup to drink from	
	Picks up pellet with pincer grasp	
13		Walks with only one hand held
		Stands unaided when placed
14	Removes cover from box in imitation	Walks unassisted
	Pushes small wheeled toy in imitation	
	Unwraps small object	
15	Cooperates in being dressed	Gets up by rolling onto abdomen
	Scribbles on paper in imitation	
	Feeds self with spoon	
	Secures and holds 3 blocks	
16	Puts object into box, in imitation	
	Puts cover on box, in imitation	
	Builds tower of 2 blocks	
	Removes pellet from bottle	
	Throws ball	
18	Reproduces pencil stroke in imitation	Takes a few steps backward
	Points out named objects in pictures	
	Builds tower of 3 blocks	
21	Points to parts of doll as named	Stands on 1 foot with help
	Builds tower of 6 blocks	Walks up and down steps, holding on
	Obtains toy by use of stick	
	Tries to turn doorknob	
24	Imitates and distinguishes between vertical and horizontal pencil strokes	Goes up steps unaided
		Gets up by turning to side
		Runs well
	Places blocks in row to make train	
	Folds paper	
	Tower of 4 blocks or more	

TABLE 4. *Special Items Needed for Developmental Appraisal, in Addition to Usual Medical Examining Equipment*

Red ring, 4″ diameter with string tied to it	1-oz. bottle
Rattle	Mirror
1″ and 2″ cube blocks	Bell
Spoon	Child's book of pictures of animals
12″ wooden stick	3″ cardboard box with top
Cup	3″ toy automobile
Saccharin or similar-sized pellets	Doll
String	Small ball, about 1″ diameter

obtainable equipment (Table 4) is needed beyond the usual office instruments and supplies. Many of the items are adapted from the work of Gesell,[12] Bayley, and Cattell,[7] to whom indebtedness is acknowledged, but no responsibility attributed, for their use in this way. Other observations have been added from personal experience and the whole organized into groups of visual responses, adaptive and imitative behavior, auditory responses and vocalization and motor accomplishments of hand function, posture and balance. This arrangement permits selection of visual and auditory responses to estimate the mental development of a baby with a motor handicap. Discrepancy between postural achievement and hand function on one hand and adaptive and responsive behavior on the other may suggest whether the major deficit is in the motor, sensory or intellectual spheres. Disproportionately poor performance in tests of visuomotor function such as form boards and peg boards may be a clue to organic cerebral disease, but interpretation of those tests requires considerable experience and should be left for the psychologist.

It should be unnecessary to add that not too much should be made of isolated test items; they should be referred to the over-all picture. What a physician sees is a minimum, not a potential, maximum, and an open mind should be maintained if the examiner's impressions do not fit reasonably well with the mother's report. One must also consider the effects of associated sensory or other handicaps, and of the baby's past experience. Physicians living in areas where competent psychological help is readily available will find relatively little need to use these scales except for babies in the first year, who are not particularly suspect and for whom no quantitative estimate is required. Such tables as 2 and 3 will be more needed in other regions, but in any event the physician should use them chiefly to determine the need for psychological consultation.

Synthesis of Findings

After the observations described have been carried out in variable order and with variable difficulty (sometimes indirectly by inspection

alone) they should be arranged systematically and their implications considered. Abnormalities may be of several types:

1. Abnormal Localizing Signs, pointing to failure of function or to release of function in some particular part of the nervous system, much as in adult neurology. These are relatively infrequent in infants, aside from convulsions.

2. Failure to Obtain Expected Responses Which Should Normally Be Present. Not too much should be made of inability to obtain a single response if all the others are normal, unless it is normally universally present (such as the Moro reflex in a full-term newborn). In any case, absence of the response should be verified on more than one occasion. Failure to obtain one supposedly invariable, or several other expected responses may reflect inadequacy of the central nervous system for function at age level, or more commonly its general depression for one reason or another.

3. Asymmetry of Normal Responses. In the neonatal period this usually indicates traumatic or anoxic insult to one side of the brain more than the other. It may be due to subdural, subarachnoid, intraventricular or intracerebral hemorrhage, especially if there are accompanying cranial nerve palsies or changes in the pupils. In later infancy, unless acute, this type of asymmetry is more often emerging evidence of a congenital hemiparesis based on porencephaly or other prenatal maldevelopment.

4. Late Persistence of Normal Signs, especially the tonic neck pattern and, to a less extent, the neck righting and Moro responses, indicates a delay in postural maturation and has a major part in a diagnosis of the cerebral palsies. Table 5 summarizes the usual timetable, but the range of normality is wide.

5. Abnormal Re-emergence of Vanished Signs usually results from a degree of motor decerebration or decortication. This may be temporary, as in infections of the central nervous system or vascular accidents, or may represent the beginning of degenerative processes such as the leukodystrophies.

6. Failure of Development is perhaps the most frequent abnormality. A distinction must be made as to whether mentality is normal and the failure based on sensory or motor disease, or whether development is equally slow in all spheres. The "clinical impression" of an experienced examiner is valuable, as may be the items in Tables 2 and 3, but the assistance of a clinical psychologist is often essential.

The ascribing of delayed maturation to motor abnormality implies the diagnosis either of some acute or progressive process or of a fixed lesion, i.e. a cerebral palsy. The predictive value of abnormal neurologic signs in the first few weeks of life is not great. Many abnormal newborns turn out to be entirely normal, although the majority of Prechtl's[25]

TABLE 5. *Normal Ages of Appearance and Disappearance of Neurologic Signs Peculiar to Infancy*

RESPONSE	AGE AT WHICH NORMALLY APPEARS	AGE AT WHICH NORMALLY NO LONGER OBTAINABLE
Spontaneous stepping	Birth	2—6 weeks[28]
Positive supporting (neonatal type)	Birth	3–6 weeks[27]
Crossed extension (allongement croisée)	Birth	1–2 months[27]
Trunk incurvation	Birth	1–2 months[27]
Moro	Birth	1–3 months[17]
Redressement du tronc	Birth	Variable[27]
Leg flexion in vertical suspension	Birth	4 months
Rooting	Birth	3–4 months awake[15] 7 months asleep[15]
Palmar grasp	Birth	6 months[28]
Adductor spread of knee jerk	Birth	7 months[3]
Plantar grasp	Birth	9–10 months[28]
Tonic neck patterns (imposable)	2 months[13]	5 months[4]
Landau	3 months[27]	12–24 months[28]
Neck righting reflex (imposable)	4–6 months	12–24 months
Positive supporting (weight bearing)	6 months	(Persists)
Parachute reaction	8–9 months[27]	Variable

abnormal neonates were still abnormal in some way at two to four years of age. It is generally only with the evolution of cortical function that congenital defects and the majority of cerebral palsies become evident. The physical signs considered most sensitive to abnormality of the corticospinal system in adults are lacking or unreliable in infancy.[30]

In congenital hemiparesis the clinical picture evolves gradually and is initially dominated by disuse and paucity of movement on one side, and by abnormal postures rather than by changes in reflexes or in muscle tone.[5] Bilateral cerebral palsy usually presents in earliest infancy as hypotonia with normal or lively reflexes, delayed motor milestones, and tonic neck patterns. The future spastic diplegias go through a stage of variable dystonic spasms followed by hypertonus relatively early.[16] Persistent clenching of the hands after four months, or extension of the legs with scissoring when suspended vertically are important clinical clues. The evolution of the extrapyramidal or future athetotic and dystonic group is more variable, since it is heterogenous. Kernicterus is a discrete subgroup which is more predictable and has been discussed elsewhere.[6]

The examiner should remember that in early infancy he is testing subcortical, central gray matter and brain stem activity. It is improbable that any neonatal activities originate in the cortex. On the other hand, the deep portions of the cerebrum must be active, for anencephalics show few of the neonatal automatisms. The trunk incurvation reflex, the anocutaneous reflex, and some effort to suck are the principal ones

present.[27–29] Focal convulsions in the first month or two do not necessarily imply cortical abnormality. In earliest infancy convulsions are clonic with little alteration in tone, and the ability to have tonic seizures may be associated with maturation of enzyme systems in the brain.[21] In synthesizing his findings the pediatrician becomes acutely aware of the limitations of physiologic knowledge concerning the nervous system in infancy. The diagnosis must still be reached largely from clinical experience, either the examiner's or the reports of others, and predictions as to the future should be made cautiously.

NEUROLOGIC EXAMINATION OF OLDER CHILDREN

Mental State

Pediatricians need scarcely be reminded to form an impression of possible retardation, depression, agitation, anxiety, hyperactivity, and so on, and of the parent-child relationship. As to neurologic disease, there are several important syndromes to recognize: Hyperactivity, distractibility, impulsiveness and short attention span are characteristic of organic brain syndromes. Depression may reflect emotional disturbance, mental retardation or parental nagging. Aloofness, lack of response to people, preoccupation with stereotyped use of objects, spinning mannerisms and deficient speech arouse suspicion of infantile autism. Some concept of the degree of the child's anxiety over his status is valuable. Patients with acute crippling diseases such as transverse myelitis are usually very upset, unless this is concealed by depression and withdrawal. Patients with muscular dystrophy, on the other hand, are characteristically little concerned about their situation in early childhood, either because of never having walked normally, with a slowly progressing disease, or because of the frequently accompanying mild mental retardation.

It is difficult to estimate intelligence except in fairly obvious cases. The need for psychological testing can be best determined by whether the child seems backward compared to its siblings or to other children of the same age. In older children, of course, progress in school is a valuable indication. Questioning as to orientation, knowledge of common facts, vocabulary, and the like, can be carried out much in the same way as with adults, but the standards naturally vary with age. Repetition of digits forward and especially backward is a valuable test of immediate memory, but the variation among children of comparable age and intelligence is proportionately greater than with adults. Drawing tests involving copying of geometric figures or reproduction of designs from memory are a field which is disproportionately disturbed in organic brain syndromes. Fragmentation of the design, failure to perceive the organization of the whole, perseveration in subparts of the pattern or confusion of background and foreground are often striking,

but the interpretation of these tests really requires a psychologist. They can be used for screening by clinicians who are experienced with them, but this should be kept to a minimum, since excessive previous testing complicates the psychologist's later efforts.

Speech

Dysarthria is best looked for casually in conversation, and a short chat is an indispensable part of an adequate examination. Dysphasia is elicited by asking the child to name common objects such as the ones which will be used later for testing stereognosis. In older children questioning should be continued down to parts of objects, such as the point of a pin, the eraser of a pencil or the hands of a watch. Substitution of other words or of definitions for the desired name may then become apparent. Receptive dysphasia is less common than nominative dysphasia, but can be tested by arranging the common objects on the table and asking the child to point to the ones named.

Praxis

Much as with adults, a child can be asked to demonstrate with his fingers how he would use scissors, brush his teeth, comb his hair, hold a pencil, feed himself with a fork, and so forth. He should also be observed during dressing and undressing later in the examination. The concept of right and left develops relatively late and variably, but children of six or seven usually know their own right and left and at eight or nine can identify right and left on the examiner or even with gloves. Gloves are also the most sensitive test for finger agnosia, ability to name the examiner's fingers and the child's own fingers coming earlier. Constructional apraxia is sought by asking the patient to make or copy a design with matches, paper clips or blocks. There may be total inability to do so or such bizarre variations as building onto a corner of the sample figure, or cannibalizing it for the new figure in preference to unused materials. The various parietal lobe phenomena have been thoroughly discussed by Critchley,[8] to whom the interested reader is referred. Testing for dysphasia and dyspraxia is extremely distressing to children who show them. It is usually wise to confine such examination to a minimum, done by a single experienced person and as infrequently as is adequate to follow the progress of the case.

Special Senses

Visual acuity can be measured with standard eye charts or with an **E** chart. Charts composed of such objects as ships, houses, and so on, are popular but less reliable, since many children find the stylized figures

difficult to recognize, particularly in the smaller sizes. Ability to locate and to name small objects at variable distances on the floor may be used for a rough test with young children. The visual fields present some difficulty, since perimetric and, particularly, tangent screen examinations can rarely be satisfactorily carried out under the age of 8 or 9 (using a slightly larger object than the usual 1- or 3-mm. white disk may help). Young children and even infants sitting on their mother's laps can be tested for binocular visual fields by bringing a small dangling object such as the steel case of a measuring tape around

Fig. 28. *A*, Testing visual fields of 4-year-old child. The dangling tape case is brought around from behind the head, and the patient turns the eyes almost automatically toward it when the peripheral limit of the visual fields is reached. *B*, Another method of testing visual fields. Child covers one eye, looks at examiner's nose and is asked to point to whichever finger moves.

the head from the back toward either side. When the limit of the visual field is reached, the child will almost invariably turn its eyes toward the object (Fig. 28, *A*). Another scheme more adaptable for testing one eye at a time is to sit opposite the child and place one's fingers at the presumed limit of the visual field on any axis. One finger, or both, is then flicked and the child asked to point at the one which moves (Fig. 28, *B*).

Hearing is tested by conversation or whispered voice or with a variety of sound-producing devices. As with the psychological status, the most that one can hope is to decide whether special testing is indicated. For infants and young children a good method is to sit opposite the patient and place both one's hands near the ears, but out of the field of vision. Snapping of the fingers or rustling of the thumb and forefinger together (this is a high-pitched sound) will usually cause turning of the head or eyes toward the side of the sound production.

Smell can be tested in the conventional manner in older children, but few of the standard odors will prove familiar. Perfume, spirits of peppermint and chocolate (the liqueur, crème de cacao, is a stable source) are the most satisfactory scents. The essential point is not whether the child can name the odor, but whether he can smell anything at all. Anosmia means little unless it is unilateral and even then is usually due to a cold or sinus infection.

Taste can be examined with the four standard flavors, sweet, sour, salty and bitter. One should first carefully explain the entire performance. The child then extends his tongue, and a drop of the test solution is placed on one side of it. He keeps the tongue out, and the examiner repeats the words, "Sweet, sour, salty, bitter," the child nodding his head when the correct one is reached. This is more satisfactory than printed cards, and testing can often be carried out down to the age of four in a bright, cooperative child. The posterior tongue can be tested for ninth nerve function with cotton applicators dipped in the solution and placed in the proper area.

Head, Neck and Spine

The head and neck are examined much as with adults. Cranial nerves are either tested formally in the conventional manner or else evaluated by observation. The entire spine should be inspected for dimples or tufts of hair which might be associated with underlying spinal cord abnormalities.

Station and Gait

This should be watched before undressing the child if he is young or apprehensive. Both walking and running should be observed and efforts

to go up and down stairs as well. Mild degrees of hemiparesis may be suspected from asymmetric associated movements of the arms in walking and running or from asymmetric sound of the footfalls. The shoes should be examined for possible unequal wear. The manner of rising from the floor is a test of particular value in muscular dystrophy, but the Gowers sign of getting up by a push on the knee is not pathognomonic of dystrophy and occurs in many other conditions with pelvic girdle weakness. The Romberg test is carried out in the standard manner. Asking a child of seven or more to stand on one foot with the eyes closed or to circle a chair in either direction may be sensitive evidence of unilateral cerebellar disease.

Motor System

The motor system is evaluated as with adults, remembering that the range of normal clumsiness is considerable. Nevertheless, differences in the skill with which the child slaps the examiner's hand with either of his own hands or in fine or alternating finger and hand movements is important. One should usually obtain a sample of the handwriting and have a few simple figures drawn with either hand.

Reflexes

Little need be said about the tendon reflexes, which can be tested much as with adults. Younger children are often best examined seated on the mother's lap, and it is better to have a child relaxed, but fully clothed, than to have him undressed on a table, but screaming and struggling. The type of reflex hammer which has a springy handle made of whale bone or solid nylon is preferable (Fig. 1). If the degree of hyporeflexia or hyperreflexia is comparable in all limbs and if there are no other abnormal findings, this may be a normal variation, the range of which is wide. The plantar reflexes usually become flexor by a year or two of age, but there is no correlation with the ability to walk.

Sensation

Touch, pin prick and temperature are tested in the usual manner. Vibration and passive movement sense are testable above the age of three if the child is bright and cooperative. The movement should be demonstrated and named while the child's eyes are open, but he should then close them for the actual testing. Stereognosis is easily tested at about the same age with common objects as in Figure 1. Other useful tests of cortical sensation are texture recognition, two-point discrimination, and the ability to name numerals written in the palm of the hand with a

fountain pen cap or other blunt object. Mapping out of areas of hypesthesia or hyperesthesia is difficult and usually requires repeated examinations, since children's span of attention for this is short. The effect of spatial or temporal summation is particularly pronounced in children, and one must test both away from and toward the supposed abnormal area. A tracing wheel of the type sold for use with sewing machines is a valuable tool, but tests both touch and pain if it is sharp.

Autonomic System

The autonomic system is usually appraised chiefly by history. Sweating and skin temperature should be assessed by touch of the examiner's hand. One should determine specifically whether a retarded child produces tears in order to rule out possible central autonomic dysfunction. Running a pin or fingernail in a line up or down the trunk will produce the triple response of blanching followed by flare and wheal. This is an axon reflex, but it may be modified by the autonomic representation in the lateral horn of the thoracic cord, for a definite level can often be shown in children with spinal cord lesions. This is an objective test which is valuable if sensory examination is unsatisfactory, but the triple response may be defective either above or below the lesion; this is also true of sweating. Sphincter function must also be appraised by history for the most part, but the tone of the anus may be examined digitally, and the anocutaneous response to pin prick is a useful sign. The question of sphincter abnormality is especially important in distinguishing paraparesis due to spinal cord lesion from the less common pure cerebral parapareses.

SUMMARY

1. Neurologic examination of infants must be done largely by observation, much of it indirectly and in unsystematic order. Many tests of localizing value are impossible, although there are special methods for some, and others may lack significance in this age group. Young infants, however, show a large number of automatisms and postural responses of which advantage may be taken for examination.

2. The commonest and most important neurologic abnormalities encountered in infancy reflect the evolution of manifestation of congenital defects, or else acute or progressive diseases which tend to involve the brain as a whole. Sharply localized vascular lesions are infrequent, and the necessarily relatively broad and nonspecific methods of testing are thus less unsatisfacory than might at first be supposed.

3. In early infancy there are only a few types of findings which are immediately indicative for treatment or further diagnostic measures.

The most important are (*a*) signs of increased intracranial pressure; (*b*) any paralysis; (*c*) anesthesia in any area; (*d*) opisthotonos or general hypertonus or hypotonus; (*e*) abnormal movements, such as convulsion, myoclonus or fasciculations; (*f*) asymmetry in tone, spontaneous movements, reflexes, cranial nerve function, or in automatisms and postural patterns; (*g*) absence of automatisms which should normally always be obtainable (except in small prematures): sucking, the Moro reflex, trunk incurvation, palmar and plantar grasp.

4. Other possible abnormal findings arouse suspicion and require careful watching or further investigation, but have less urgency and may be of poor predictive value. These are (*a*) absence of automatisms to be expected at the patient's maturity, particularly if several are missing. (In early infancy: rooting, movement of head to touch, resistance to frontal and occipital pressure, traction response, stepping, placing, *allongement croisée, redressement du tronc.*) (*b*) Abnormally late persistence or re-emergence of postural patterns which ought to have disappeared. (The tonic neck reflex is the most important of these.) (*c*) Abnormal postures in vertical and horizontal suspension. (*d*) Delayed development or regression.

5. Methods of examination of infants are described for the abnormalities listed.

6. Neurologic examination of older children differs little from that of adults except in standards of normal for some items, and in the need for special methods for a few tests, which are discussed.

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DEVELOPMENT OF POSTURAL AND TONIC PATTERNS IN THE NEWBORN INFANT

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The purpose of this investigation is to define clinically the termination of what we call the newborn period. Philosophically, the question may be put in the following manner: When does the infant begin to live as an independent organism not subjected to the parasitism that conditioned his intrauterine life? The answer to that would be: When he accepts fighting against gravity. This "fight," characterized by a series of postural and tonic situations, can be systematized by neurologic examination. The time that elapses between the moment of birth and the adoption of an independent tonic-antigravity conduct is variable and appears to be fundamentally influenced by obstetrical factors and by the state of health and nutrition of the mother. Since psychological maternal preparation for birth appears to eliminate this interval, one may assume with good foundation that the so-called shock of the newborn infant is not a *sine qua non* condition of birth, but is rather the result of the aberrations and deformations that civilization has imposed upon the mother-child relationship at the moment of birth. It is the purpose of this work to study this situation.

MATERIAL

Only clinically sound infants from normal pregnancies and births were selected for this study.

The first group, used as controls and including 165 infants born by spontaneous, noninstrumental delivery, were subjected to 285 complete

neurologic examinations. Only oxytocics or antispasmodics had been administered before delivery to the mothers.

A second group of 33 newborn infants, from a similar socio-economic background to those in the control group, was also studied. The mothers of these infants underwent periodic check-ups by their obstetricians and followed prescribed exercises and courses in psychoprophylaxis ("painless childbirth") from approximately the seventh month onward. Sixty-five neurologic examinations were performed in this group.

A third group included 44 healthy newborns delivered cephalically by goitrous mothers. Each mother in this group had enlargement of the thyroid gland: one fourth had the nodular type of goiter and the rest the diffuse variety. They were native to a zone in northeast Argentina where goiter is endemic and were delivered at the Model Maternity Clinic of the Province of Salta. A total of 107 neurologic examinations were carried out on this group.

A fourth group included 20 infants of healthy mothers of the same socio-economic background, born in the same Maternity Clinic as the infants in group 3.

Infants less than 2700 gm. at birth were rejected in order to exclude those who might show the characteristic postural attitudes of the premature, which are somewhat different from those of the full-term infant.

Infants born by face or breech presentation were also excluded from our study because, without being abnormal, they may evince distinct postural attitudes.

METHODS

The infants were examined when they were awake or during the semi-wakefulness characteristic of the first days of life. During sleep there is a complete hypotonia that influences the results of an examination of posture. The same phenomenon occurs after nursing when the infant is sated.

The infant should be quiet, because crying increases muscular tension. During the first days most infants demonstrate less hypotonicity when crying. For this reason it is best not to examine them shortly before their nursing period.

The examinations were carried out at a comfortable room temperature (22° C.) with the baby completely naked in order to observe his total reactions after each test.

Each test was repeated several times in order to form a definite opinion about the neurologic behavior of each infant, since, at times, there may be different responses to identical stimuli. Careful observation

is required to evaluate the tonic and postural patterns and the reflexes of the newborn infant.

The manipulations were as gentle as possible. Procedures that might irritate the infant or provoke a crying spell, such as suspension by the feet, supporting him horizontally under his back, or the Moro reflex, were left for the end.

Each examination was performed on a lightly quilted cot or table with a firm surface, since a soft surface tends to mold to the body of the infant, thus hiding his true posture.

RESULTS AND OBSERVATIONS

Neurologic Findings During Birth Shock

MUSCLE TONE. The *consistency*, tested by digital palpation of the muscular masses, is poor during this period. Although it is not as extreme as the buttery consistency found in pathologic cases of shock, atonia or mongolism, the sensation is similar to feeling a feather quilt or overripe fruit.

During the birth shock the *resistance to movement* is minimal; the arms and legs can be passively extended, and they then slowly return to their normal position of flexion. Shaking the distal segments of the extremities (ballottement) elicits wide ranges of movement even when the infant cries. Moving the trunk causes maximal cephalic rolling.

The extensibility or ranges of both flexion and extension, as well as of internal and external rotation, adduction and abduction of the four extremities, is also maximal in this period. The most objective test is measurement of the popliteal angle; with the newborn infant lying on his back, the thighs are flexed over the abdomen and the widest possible opening of the popliteal angle is measured. During the first days of life this angle reaches nearly 180 degrees; the feet can reach the mouth or even the ears (Fig. 29, *left*).

POSTURAL ATTITUDES. The body positions of the pretonic newborn infant in its first days have fundamental features that are repeated, with specific characteristics, in each position; absence of the battle against gravity is evident, with a tendency to abduction and, at times, semi-extension (Fig. 30, *left*).

In the dorsal decubitus, absence of the fight against gravity manifests itself by complete contact of all segments of the body with the cot; the back molds itself to any surface, and whether the arms are abducted or not, the flexed forearms lie on the bed, the hands resting on both sides of the head. The legs may be extended or flexed-abducted. In this latter position it is the lateral surface of the thighs that rests on the cot. The head is invariably turned to one side because, during this period of life,

the tonic neck reflex does not determine the attitude of flexion or extension of the arms as it will later.

When the newborn infant is seated with head and trunk in a vertical plane and then is suddenly left without support, his head falls forward and is followed by the trunk (Fig. 31, *left*). In extreme cases of shock the head falls between the feet and the lax arms are extended on both sides of the trunk. The legs are extended and slightly abducted. Reflex actions or crying does not modify this posture. However, when hypotonia is not too great, the infant left in this position begins to perform movements tending to return his limbs to a state of flexion; he arches his back and frees his legs from under his pelvis, and adopts the ventral decubitus.

The infant is next examined in the ventral decubitus. His head always turns to one side until the nostrils are free because the tonic neck reflex impedes his maintaining it in the midline. This movement may be fast or slow, laborious or delayed, but only very sick infants fail to perform it. The trunk is in complete contact with the cot; the arms may be abducted to a 90-degree angle and rest on the examining table; the forearms and hands are kept lightly flexed. The legs may be extended or slightly abducted with maximum separation at the level of the knees, or they may be completely abducted and flexed like those of a frog (Fig. 32, *left*). Regardless of the leg position, there is scarcely any elevation of the pelvis, so that creeping movements occur only when the soles impinge on firm support.

Maintaining the infant erect by supporting him under the armpits brings out either a weak reaction or none at all. The same is true when he is held in walking position (Fig. 33, *left*). In this position there is a tendency for the head to fall forward.

When the infant is held horizontally face down and supported by the abdomen, the trunk curves in flexion and the head drops (Fig. 34, *left*). The arms and legs also tend to drop, although a certain degree of flexion is retained.

By reversing this position to have the back of the infant downwards, the curvature of the trunk becomes more pronounced (Fig. 35, *left*); the head falls almost pendulously because of the absence of the antigravitational reaction of the anterior neck muscles. The arms are maintained in flexion and adduction in contrast to the legs, which tend to extend to a semi-flexed position.

When the baby is suspended by the feet (Fig. 36, *left*), the popliteal angle tends to decrease or disappear, and the legs, thighs, trunk and head form an almost straight line. The arms tend to fall, attenuating the flexion and adduction.

Reflexes. The pattern of reflexes of the newborn infant during the period of birth shock is variable. Some reflexes, such as the "Japanese

doll eyes" (A. Thomas), the patellar and contralateral patellar, and plantar prehension, are present from the first moment of life with the same vigor as in infants several days old. Others, on the contrary, are absent or very weak.

The time of establishment of the oral reflexes is variable, but as a rule they do not reach their maximum intensity until 24 to 48 hours of age. The newborn does suck a nipple introduced into his mouth, but oral searching (the four cardinal points of A. Thomas) is weak and ill defined.

The embrace response in the arms (Moro reflex) is present from the first moment of life. But the reaction is slow and incomplete until the shock period is over (total extension and abduction of the arms from the shoulder to the fingers are not obtained, but only a rapid jerk with quick separation of the arms). The response is identical no matter which stimulus is used: hitting the table, sudden raising of the pelvis, percussion of the sternum, and so forth.

Palmar prehension (grasping) can be so strong and intense that the newborn infant can support his own weight for several seconds by grasping the examiner's fingers. But commonly the reflex is weak and disappears when one tries to seat the infant by means of his own grasp reflex.

The abdominal reflexes can be diffuse, localized, asymmetrical and frequently absent. This wide range does not disappear in the days after birth, and therefore they were not considered in this study.

The trunk curvature response (A. Thomas), like the crossed arms and grasp reflexes, is customarily present from birth, but the response is weak, and at times it is necessary to perform several stimulations. To elicit its response the newborn infant is placed on his face and the lumbocostal zone is stimulated with a blunt stylus.

The plantar defense reflex can be elicited with the same instrument. This reflex is weak during birth shock, but rapidly acquires its characteristic withdrawal response of flexion and retraction of all segments of the lower extremity.

Impeding the withdrawal response by maintaining the knee fixed while stimulating the sole gives a metameric response: the crossed-extension reflex, which consists in flexion followed by extension and adduction of the opposite leg. The intensity of this response is usually parallel to that of the defense reflex and is generally established from the first day, although occasionally it is slow and incomplete.

The cutaneous plantar reflex is obtained by lineal stimulation of the sole, from the heel to the toes, with a blunt stylus or by tickling the outside border of the dorsal surface of the foot (Collin). The response is weak in one fourth of the infants during the birth shock period. The responses are variable: extension of the toes, flexion with or without

abduction of the first toe in a fanlike movement, and so on. We consider all the responses normal if they are symmetrical. The presence and intensity of the reaction are also taken into account for the purpose of evaluation.

During the birth shock period the newborn infant is in a state of somnolence close to coma. It is difficult to wake him, and even in the brief moments when his eyes are open his reactions are slow. Some newborn infants may have a transitory period, lasting five or six hours after delivery, in which they are excited and irritable, cry and occasionally engage in vigorous reflex activity.

Neurologic Findings after Birth

Forty-eight to 72 hours after birth the neurologic behavior of the newborn infant changes rapidly and progressively.

Muscle Tone. Muscle tone increases and, by the fourth or fifth day, takes on the characteristics of maximal tonicity typical of the suckling infant of the first three months of life. The muscular masses become firmer in *consistency* and are not readily dented by the palpating finger.

Resistance to movement is manifested by the difficulty encountered in passively extending the extremities, which return, like springs, to their flexed position as soon as they are released. There is practically no swinging of the hands or feet when the forearms and legs are shaken (ballottement).

Extensibility likewise diminishes commensurate with this resistance. The maximum opening of the popliteal angle does not surpass 90 to 100 degrees (Fig. 29, *right*).

Postural Attitudes. The postural attitudes of the newborn infant also change after the period of birth shock, and these new attitudes will be maintained during the first three months of life.

In every lying position the posture is characterized by an active battle against gravity with flexor tone predominant and a tendency to adduction of the extremities.

In dorsal decubitus (Fig. 30, *right*) the newborn has a tendency to opisthotonos. Rotation of the head frequently forces the infant to a semilateral position. The arms are kept adducted and flexed and at no point make contact with the bed. They adopt a symmetrical position interrupted occasionally by the tonic neck reflex. The legs are maintained in flexion and adduction, and only at times do the heels contact the bed.

By holding the infant in a sitting position and then suddenly releasing him, one can observe slight cephalic swaying. The head no longer inevitably falls forward; it is more likely to drop backwards, owing to increase in muscle tone of the neck extensor muscles (Fig. 31, *right*).

Another factor influencing this extensor reaction is that the legs, hyperflexed against the abdomen, impede the forward fall. The arms play no role, being maintained in flexion with the elbows slightly backwards.

If infants who adopt the postural attitude just described are made

Fig. 29. Popliteal angle and leg position of the newborn infant during the stage of birth shock (*left*) and after this period (*right*).

Fig. 30. Posture in dorsal decubitus during the period of birth shock (*left*) and after this period (*right*).

to fall forward, they do so, but extensibility of the back is so poor that it does not stretch to sufficient length to maintain this position, and after several seconds the pelvis is raised to permit the flexed legs to move backward, thereby enabling the infant to attain the ventral decubitus.

The newborn infant who is over the birth shock adopts a character-

istic posture when lying on his stomach (Fig. 32, *right*); the head is rotated to one side either by dragging it or by a fleeting moment of elevation, thus leaving the nostrils free. The head and thorax contact the bed, but the abdomen and pelvis remain raised because of hypertonicity

Fig. 31. Head and trunk response in the sitting position during the period of birth shock (*left*) and after this period (*right*).

Fig. 32. Posture in ventral decubitus of infant during the period of birth shock (*left*) and after this period (*right*).

of the dorsal muscles and the flexion of the legs, which are held in a kneeling position. Either spontaneously or in response to firm pressure on the soles of the feet, the infant performs rhythmic movements of pulling and creeping which are precursors of the crawling activities in later infancy. The arms remain adducted with elbows back without

touching the bed. The infant raises his thorax by bearing down on his forearms and hands.

Contact of the soles with a firm surface brings forth the reaction of support and straightening (Fig. 33, *right*) with an extensor reflex which is sometimes so complete that the infant arches backward in opisthotonos. If at this moment the infant is given a light push forward, he starts rhythmic and reciprocal motions of gait wherein the feet have a tendency to scissor because of the hypertonia of the hip adductors. The heel of the foot makes contact with the table. There may be excessive flexion of the knee and hip joints. As soon as the propulsion stops, this

Fig. 33. Support reaction of the infant during the period of birth shock (*left*) and after this period (*right*).

walking reflex also stops. This automatic or primary reflex is the precursor of the definitive support and prewalking reflexes of the second half of the first year.

If the infant is suspended by his abdomen, the trunk does not assume a flexed curve, but the head is either kept in a straight line or is raised (Fig. 34, *right*). This is one of the best tests to demonstrate the postural antigravity action. The arms and legs extend to a less degree than during birth shock and maintain a flexed position.

When he is suspended in the supine position, there is less arching of the back, and head drop is minimal or absent. The limbs clearly maintain their position of flexion-adduction (Fig. 35, *right*).

When he is suspended by the feet, the popliteal angle cannot be distended more than 150 to 160 degrees (Fig. 36, *right*); the trunk and

head form a slight concave arch; the arms do not drop, but are kept in flexion.

REFLEXES. The reflexes acquire a strength in their responses that is typical of centrencephalic rather than of cortical control.

Except for the "doll eyes" reflex, the curvature of the trunk and the

Fig. 34. Posture response to prone suspension during the period of birth shock (*left*) and after this period (*right*).

Fig. 35. Posture response to supine suspension during the period of birth shock (*left*) and after this period (*right*).

crossed extensor reflexes, which disappear between the twentieth and fortieth days, the reflex responses of the infant who has surmounted the birth-shock period are the same during the entire first three months.

The reflex of the "Japanese doll" eyes, characteristic of poor ocular-cephalic coordination, is as intense as in the first hours of life, but even more clearly seen because it is now possible to observe the infant with his eyes wide open.

After the first 48 hours of life the oral reflexes are fully established, and the hungry infant follows orally the four cardinal points.

The embrace reflex of the arms gives a clear response, and not infrequently manipulation of the baby or a sudden noise will bring it forth.

The palmar grasping reflex is energetic and constant. It is possible to sustain the infant in the air for 10 to 30 seconds.

The trunk curving response may be constant and strong. The concavity of the spinal column may be maintained for several seconds.

The plantar reflexes are clearly and strongly elicited.

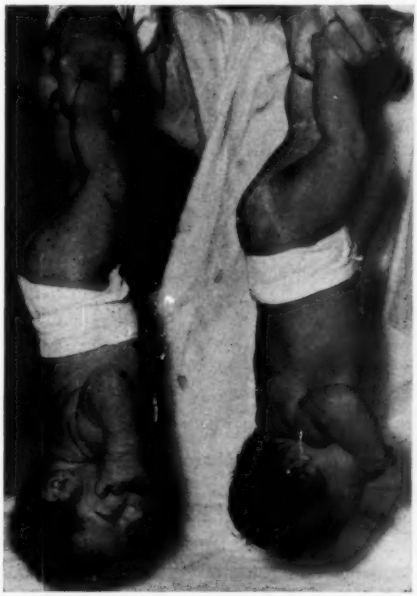

Fig. 36. Posture response to suspension by the feet during the period of birth shock (*left*) and after this period (*right*).

When the period of shock is over, the sleepiness of the newborn infant gradually disappears, and there are moments when he is fully awake, especially when the feeding hour approaches. At this age differences of reaction that distinguish one temperament from another begin to be noticeable, and the family or hospital environment becomes an influential factor.

OTHER GROUPS STUDIED

Newborn infants delivered to mothers prepared prenatally by the psychoprophylactic method ("painless childbirth") show, from the first day,

neurologic characteristics generally shown by infants in the second stage of their neonatal period (i.e. after the birth shock is over). These infants do not pass through the phase of hypotonus and inhibition of the cutaneous and postural reflexes which are considered physiological in infants born by ordinary obstetrical practices. A newborn infant delivered by "painless childbirth" is in its first 24 hours homologous to a 4-day old infant born by customary methods (Fig. 37).

Undernourishment of the mother during pregnancy appears to increase the intensity and duration of the period of neurologic birth shock. We have observed newborn infants whose mothers had received during their pregnancy diets made up solely of carbohydrate, without proteins or vitamins. Their infants, although of normal length and weight, were hypotonic and their postural attitudes at the lower limit of normal.

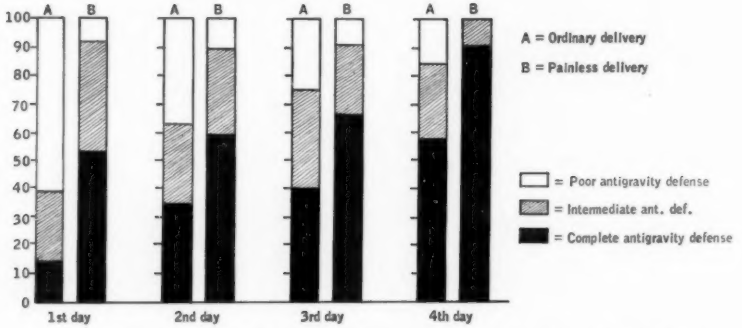

Fig. 37. Postural attitudes of the newborn as expressed in antigravity defenses.

On the fourth day of life they still had not totally lost these characteristics.

In a zone in northeast Argentina where goiter is endemic, we found the neurologic shock at birth to be greater in the newborn infants of goitrous untreated mothers, while the controls, i.e. infants of nongoitrous mothers of the same ethnic and socio-economic group, were the same as the newborn infants from ordinary deliveries, studied in the maternity clinics of Buenos Aires.

TABULATION

A value of 0 is conventionally allotted to the total absence of fight against gravity, 1 to slight responses, 2 to intermediate postures, and 3 to strong antigravitational attitudes. Each value is an average of a series of several observations of each child on a given day of his neonatal period. The mean is calculated for each day from the values obtained

TABLE 6. *Evolution of Postural Attitudes of the Newborn Infant* (Ordinary Delivery)*

	1ST DAY	2ND DAY	3RD DAY	4TH DAY
Mean values	1.53	1.86	2.25	2.42
Standard deviation	0.50	0.54	0.44	0.40
Number of infants	50	48	40	31

* Based on value of 0 for no antigravity response, 1 for slight, 2 for moderate, and 3 for strong antigravity response.

for each infant. In this manner four average values were obtained for the first four days.

In order to show the large variation of individual values, the standard deviations were calculated and are shown in Table 6.

Tables 7 and 8 show the absolute values for the whole group obtained by totalling for each day the number of neurologic findings corresponding to each class of tonic behavior. The percentage figures point out more clearly the increase in antigravitational attitudes in the course of the first four days. They also show the day-by-day differences between the infants born through painless childbirth and those of goitrous mothers and those of healthy mothers of the same socio-economic status.

COMMENT

Every baby undergoes, immediately after birth and for a period ranging from 24 to 60 hours thereafter, a period of neurologic shock which has always been considered physiological. If this is due to a temporary inhibition of the normal functions of the nervous system incident to anoxia and trauma during delivery, it seems logical to assume that decreasing the anoxia and the traumatizing mechanical factors should diminish and even eliminate this inhibitory phase.

Our studies demonstrate clearly that neonatal shock can be eliminated or considerably diminished (in both intensity and duration) if appropriate psychoprophylactic care is given to the mother during pregnancy.

The psychoprophylactic method consists in the establishment of conditioned reflexes pertaining to delivery which tend to inhibit painful reactions. The mother can concentrate and consciously direct her muscular efforts without fear, thereby shortening the uterine contractions that impinge against the body and especially the head of the infant. This may be the basis of the benefit of the "painless childbirth" method to the infant.

Other possible factors are the decrease in muscular tension of all the ancillary muscles, better oxygenation because of better respiratory control, the avoidance of sedatives and anesthetics and, perhaps, the

TABLE 7. *Evolution of Muscular Tone in the Newborn Infant*

TONE	ORDINARY DELIVERY								"PAINLESS CHILDBIRTH"							
	1st Day		2nd Day		3rd Day		4th Day		1st Day		2nd Day		3rd Day		4th Day	
	No.*	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Poor	107	65	63	42	29	26	22	23	1	3	5	12	—	—	—	—
Intermediate	19	11	32	22	21	18	25	26	6	19	8	20	3	7	4	13
Elevated	39	24	53	36	62	56	49	51	26	78	26	68	42	93	26	87
Totals	165	100	148	100	112	100	96	100	33	100	39	100	45	100	30	100

* Number of signs.

TABLE 8. *Muscle Tone of Newborn Infants of Goitrous Mothers and of Healthy Mothers*

TONE	GOITROUS MOTHERS								HEALTHY MOTHERS							
	1st Day		2nd Day		3rd Day		4th Day		1st Day		2nd Day		3rd Day		4th Day	
	No.*	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Poor	42	58	27	44	27	36	28	37	6	20	3	96	2	7	4	15
Intermediate	20	28	20	32	27	36	29	39	13	43	18	55	15	50	11	40
Elevated	10	14	15	24	21	28	18	24	11	37	13	36	13	43	12	44
Totals	72	100	62	100	75	100	75	100	30	100	33	100	30	100	27	100

* Number of signs.

improved emotional attitude of the mother which may directly stimulate the receptors of the infant, thus influencing the activity of his central nervous system from early intrauterine life.

Just as intensification of the birth shock to pathologic limits may threaten the neurologic future of the newborn, so the lessening or removal of this shock may assure a better prognosis. If the neurophysiologic maturity of infants born by "painless childbirth" is shown to be superior to that of infants born by orthodox methods, it will be wrong to apply the term "physiological" to the manifestations of shock during the first days of life.

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ENZYME DETERMINATIONS IN NEUROLOGIC AND NEUROMUSCULAR DISEASES OF INFANCY AND CHILDHOOD

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Diagnostic considerations in the sphere of neurologic diseases are usually derived from pertinent history and physical findings with but limited guidance afforded by laboratory procedures. The classic biochemical techniques used with advantage in somatic diseases have but limited value in the diagnosis of primary nervous system disorders. In recent years the clinical applicability of quantitative enzyme activity in biologic fluids has been explored extensively, particularly in relation to hepatic, myocardial and neoplastic disturbances. Through this avenue of approach a battery of sensitive tests has been evolved, often with notable diagnostic and prognostic utility. At present these tests are being applied to primary neurologic and neuromuscular disorders.

The concept that certain disease states can be detected by altered enzyme activity in serum and cerebrospinal fluid rests upon a number of assumptions. Intracellular metabolism is, essentially, a collective chain of successive biochemical transformations, each mediated by highly specific biologic catalysts. The continuance of cell life is dependent upon uninterrupted activity of these agents.[9] Destruction or serious physiologic impairment of selective tissues may, therefore, liberate the intracellular enzymes into the most readily accessible biologic fluid. Although most enzymes can be found in all cells, there is considerable variation in their relative concentrations. This quantitative difference, under normal circumstances, is a reflection of metabolic specialization. Since the intracellular enzymes have no known function within serum

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or cerebrospinal fluid, it can be assumed that the enzymatic content normally found in such circulating fluids represents enzyme in transit from cells and that the source of these enzymes is probably a combination of continuing intracellular biosynthesis and normal cell replacement. A rise in the circulating content of a specific enzyme can therefore be construed as a signal of necrobiosis or functional damage in such tissues characterized by a differentially elevated concentration of the particular enzyme. The specifically responsible tissue cannot always be adduced, but with judicious assessment of the associated clinical data a reasonable localization is possible. At times the nature of the pathologic process also can be inferred.

In the majority of instances the weight of evidence indicates that an abnormal elevation in serum or cerebrospinal fluid enzyme activity represents a release from pathologically altered cells rather than an increased biosynthesis. Under experimental circumstances it can be shown that the *circulating fluid* enzyme increase is closely associated with diminishing *tissue* enzyme levels (e.g. induced myocardial or cerebral infarction in laboratory animals). As experimentally provoked tissue degeneration persists, the serum enzyme level returns to normal, indicating an exhaustion of the primary source of additional circulating enzyme. Generally the elevation tends to be transient, and the highest values are recorded at the onset of the destructive process. They therefore do not usually coincide with the time of most profound tissue damage.

In malignant neoplasms characterized by intense cellular reproduction, accelerated enzyme release may follow more active intracellular synthesis. Under such circumstances it would not be necessary to assume the existence of any tissue necrosis.

A *sustained* elevation of enzyme activity is uncommonly encountered and when noted often presages a continuing cell degeneration progressively incorporating previously unaffected tissues. Serial enzyme determinations are therefore of distinct prognostic value serving to indicate the quantitative extent of acute tissue damage (by the magnitude of the initial peak in enzyme activity) and extension of the destructive lesion (by the endurance of abnormally elevated enzyme activity).

Of further concern in clinical enzyme activity interpretation is the velocity of the basic pathologic process. Since a combination of factors such as rate of liberation, degree of subsequent inactivation and rate of excretion will collectively determine the level of circulating enzyme, it is apparent that an equilibrium can still be maintained if the *rate* of enzyme liberation is sufficiently slow. A situation analogous to this is found in many of the chronically progressive nervous system abiotrophies of childhood. In these illnesses there is usually no detectable fluid enzyme change; and though considerable destruction of neural tissue is

found at the termination of the disease, only a small amount of tissue is impaired in any unit of time, thus not appreciably taxing the kinetics of circulating enzyme content.

Of the more than 500 enzymes whose catalytic function has been described, only a small number have been used as indicators of neurologic disease states. The studies of altered enzyme activity have been confined principally to the cerebrospinal fluid. In most intracranial diseases the serum levels of these catalytic substances have been unaffected. The blood-brain barrier is apparently of sufficient impenetrance to prevent an enzyme elevation in either serum or cerebrospinal fluid from being mirrored in the alternate fluid. Under rare circumstances, when the liberation of enzymes from brain tissue is massive and enduring (as in infantile amaurotic family idiocy), this threshold may be exceeded.

METHODS

The units of enzyme measurement do not represent the actual amount of enzyme, but rather reflect the extent of enzyme activity as determined by the amount of introduced substrate catalytically transformed in a given period of time. The concentration of enzyme is therefore determined by indirection. The units of activity are often defined as an arbitrarily chosen amount of optical density change, as measured spectrophotometrically, in a specified time. Colorimetric and turbidometric techniques are also used when warranted. The true amount of enzyme is exceedingly small (e.g. less than 5 mg. of pure aldolase is present in the total blood volume). The precise methods used may be found in the various references cited.

Numerous precautions must be observed in fluid or tissue techniques for enzyme determination.[6, 18] The concentration of many enzymes, particularly those of glycolytic function, is many times higher in erythrocytes than in serum. A specimen of serum contaminated by hemolysis is therefore of no interpretive value, since the breakdown of red blood cells causes a striking elevation of enzyme in the serum. The interval must be brief, since enzymes deteriorate with time even under refrigeration. Enzymes are also susceptible to inactivation by heat, various organic reagents and metal cations. It is also essential that biophysical conditions in the reacting solutions be constant and reproduceable and closely approximate the circumstances wherein the enzyme is most stable (e.g. temperature, dilution and pH).

Cerebrospinal fluid derived from direct lumbar puncture is preferable to fluid obtained after pneumoencephalography, since preliminary introduction of air abnormally elevates the levels of cerebrospinal fluid enzymes.

TABLE 9. *Enzymes Commonly Used in the Diagnosis of Neurologic and Neuromuscular Diseases*

ENZYME	INTERCONVERSION	NORMAL RANGE (UNITS)
Aldolase	Fructose-1-6-diphosphate ⇌ dihydroxyacetone phosphate + glyceraldehyde-3-phosphate	Serum : 3–0 CSF* : 0–1
Phosphohexose isomerase (PHI)	Glucose-6-phosphate ⇌ fructose-6-phosphate	Serum: 8–40 CSF : 0–4.2
Glutamic oxalacetic transaminase (GOT)	Aspartate + *a* ketoglutarate ⇌ glutamate + oxalacetate	Serum: 10–40 CSF : 4–14
Glutamic pyruvic transaminase (GPT)	*a* Ketoglutarate + alanine ⇌ glutamate + pyruvate	Serum: 10–45 CSF : 5–15 (?)
Lactic dehydrogenase (LD)	Lactate + DPN† ⇌ pyruvate + (DPN.H + H^+)†	Serum: 100–600 CSF : 5–40
Malic dehydrogenase (MD)	Malate + DPN ⇌ oxalacetate + DPN.H + H^+	Serum: 42–195 CSF : 10– 25
Isocitric dehydrogenase (ICD)	Isocitrate + TPN‡ ⇌ *a* ketoglutarate + (TPN.H + H^+)‡	Serum: 47 –264 CSF : 1.7–11.9
Glutathione reductase	Glutathione (oxidized) + TPN.H + H^+ ⇌ glutathione (reduced) + TPN	Serum: 10–70 CSF : 1–10

* Cerebrospinal fluid.
† Diphosphopyridine nucleotide, oxidized and reduced forms.
‡ Triphosphopyridine nucleotide, oxidized and reduced forms.

CENTRAL NERVOUS SYSTEM NEOPLASMS

The usefulness of enzyme levels in patients with neoplasia has been extensively explored and constitutes one of the first practical clinical applications of the phosphomonoesterase and glycolytic enzyme assays.[18, 29]

Serum enzyme activity (GOT, LD, aldolase) is normal in neoplasms confined to the cranial cavity.[3, 12, 33] Evaluation of cerebrospinal fluid, however, has often shown perceptible increases in the activity of some enzymes, occasionally in approximate accordance with the degree of cytologic malignancy.

Many factors in brain tumors are capable of modifying the appearance and extent of increased enzyme release into cerebrospinal fluid. Neoplasms impinging upon or invading either the leptomeninges or ventricular ependyma are more apt to produce abnormal values than those neoplasms which are situated more deeply. Tumors extrinsic to the dura mater have not caused any change in cerebrospinal fluid enzyme levels. Brain tumors coexistent with obstructive hydrocephalus are more apt to influence the cerebrospinal fluid level of GOT (glutamic oxalacetic transaminase).[23] If, on the other hand, the neoplasm is instrumental in causing complete obstruction, the increased enzyme activity may not reach the general cerebrospinal fluid reservoir.[39]

Since the normal concentration of most enzymes is appreciably higher in serum and erythrocytes than in cerebrospinal fluid, any pathologic process causing subarachnoid or ventricular bleeding will significantly elevate the enzyme content within cerebrospinal fluid. No positive correlation, however, has ever been shown between cerebrospinal fluid enzyme levels and the relative variations in cerebrospinal fluid glucose, protein or chloride content.[40]

The diagnostic value of repeated cerebrospinal fluid enzyme determinations assumes particular importance in those instances in which the choice between neoplasm and cerebral infarction cannot be decided by clinical means alone. Although both types of lesions may result in enzyme elevations, there usually is a prompt remission of values after infarction. On the other hand, if certain enzymes in cerebrospinal fluid rise because of an intrinsic neoplasm, the rise is generally sustained unless specific therapeutic agents are introduced.

Gliomas

The GOT and LD (lactic dehydrogenase) levels in cerebrospinal fluid have been reported to be affected by the presence of verified gliomas, regardless of the degree of cytologic anaplasia.[12, 15, 16, 23, 33, 39, 41] Other observers have recorded occasional rises in cerebrospinal fluid GOT.[7, 13]

Thompson and his associates[32] have also reported that cerebrospinal fluid PHI (phosphohexose isomerase) is increased in most instances of glioblastoma multiforme and medulloblastoma, but within the range of normal activity in the presence of most benign astrocytomas.[32] In this regard it is interesting to note that the cellular content of PHI is greater in component cells of glioblastoma than in the cells of astrocytoma.[26]

The activity of cerebrospinal fluid ribonuclease is distinctly increased in patients harboring intracranial neoplasms, regardless of histologic type.[13] The degree of increase seems to bear no correspondence to the degree of malignancy.

Nongliogenous Primary Neoplasms

Meningiomas, unassociated with any bleeding episodes, have not caused abnormalities in any of the enzymes extensively assessed (GOT, LD, PHI).[3, 12, 15, 32, 33] Similarly, normal cerebrospinal fluid enzyme levels have been recorded in craniopharyngioma, pituitary tumors and intracranial neurinomas.

Metastatic Neoplasms

The cerebrospinal fluid activity of ICD (isocitric dehydrogenase) and PHI is significantly increased in cases with neoplasms which have metastasized to the brain.[32, 33] Cerebrospinal fluid LD is also consistently elevated in leukemic, lymphomatous and carcinomatous invasion of the nervous system. Neuroblastoma of infancy, metastatic to the brain, causes a similar change.[39] Wroblewski[40] has noted that abnormal enzyme values revert to normal after temporarily successful therapy of the leukemias.[40]

It has been suggested that cerebrospinal fluid LD can be of aid in distinguishing primary from secondary intracranial neoplasms on the basis of the elevated values equated only with the latter.

INFECTIOUS DISEASES OF THE NERVOUS SYSTEM

A limited number of studies have applied enzymologic techniques to the diagnostic problems of nervous system infections. Since the endogenous enzyme content of circulating leukocytes is considerable, it is probable that the incremented cerebrospinal fluid levels of the enzymes, particularly those of glycolytic function, can be traced to the reactive white blood cells in cerebrospinal fluid. In confirmation of this, Green and associates[12] were able to abolish the usually elevated cerebrospinal fluid GOT levels in specimens derived from patients with meningitis

by prior, vigorous centrifugation. Wroblewski[39] has offered the view that acute infections of the leptomeninges sufficiently alter the hemoencephalic barrier so as to permit passage into cerebrospinal fluid of serum protein and particularly the globulin fraction (the locus of much of the extracellular enzyme). Kovacs[19] thought it possible that the incremented enzyme levels in leptomeningitis may be partly derived from the invasive pathogens.[19]

Acute Bacterial Leptomeningitis

Dramatic elevation of cerebrospinal fluid LD, ICD, PHI, GOT and aldolase has been described in the acute phases of suppurative leptomeningitis.[12, 15, 16, 32, 33,39] Regression to normal values generally accompanies appropriate therapy. The initially abnormal values are often three to six times greater than normal. Cerebrospinal fluid ribonuclease is demonstrably elevated in leptomeningeal infections, probably reflecting the considerable amount of this enzyme elaborated by leukocytes.[13] Glutathione reductase content of cerebrospinal fluid is also elevated in acute meningitis, as determined in a limited number of cases.[22]

Chronic Infections of the Nervous System

In one case of tuberculous meningitis, under active treatment, the cerebrospinal fluid PHI content was normal.[32] In untreated, active cases of tuberculosis of the leptomeninges cerebrospinal fluid LD is elevated, but not to the degree exhibited in purulent infections of the meninges. Serial cerebrospinal fluid determinations in patients treated with streptomycin and para-aminosalicylic acid have demonstrated a prompt remission of the abnormal LD levels weeks before any perceptible reversion of other cerebrospinal fluid criteria (e.g. protein content, cell count, and so on).[40] LD and GOT levels in cerebrospinal fluid have not deviated from normal in congenital or acquired neurosyphilis, regardless of whether or not therapy had been instituted.[7, 33] In an isolated case of acute cryptococcal meningitis a dramatically elevated cerebrospinal fluid PHI was reported.[32] This enzyme was unchanged in various other forms of chronic leptomeningitis.

Viral Infections of the Nervous System

A high PHI content in cerebrospinal fluid has been noted in the initial phase of acute poliomyelitis.[32] None of the enzymes previously considered (LD, GOT) have been shown to be altered during the convalescent phase of this illness. Normal cerebrospinal fluid GOT values

were obtained in cases of viral encephalitis when the number of leukocytes did not exceed 50 per cubic millimeter.[12] Cerebrospinal fluid elevations of PHI have been reported in viral encephalidites, but are independent of the extent of cerebrospinal fluid pleocytosis.[32] No cerebrospinal fluid GOT changes have been recorded in the Guillain-Barré syndrome.[7]

In samples of normal cerebrospinal fluid measurable activity of desoxyribonuclease usually cannot be demonstrated. Some degree of activity is exhibited in most cases of septic meningitis, but none in the meningoencephalidites of viral etiology.[19]

VASCULAR DISEASES OF THE NERVOUS SYSTEM

Experimental animals subjected to temporary cerebral anoxia showed increased amounts of cerebrospinal fluid GOT within hours after tissue insult.[36] Elevated cerebrospinal fluid GOT has been found in the majority of patients with cerebral infarction, although the peak of elevation is not achieved until two to three days after clinical onset of the cerebral vascular episode.[7, 12, 23] The magnitude of primary increase in activity is almost directly proportionate to the volume of neural tissue affected. High levels are not sustained unless additional intracerebral areas become incorporated into the encephalomalacia. These clinical-enzymologic relations have also been demonstrated with ICD and, to a less degree, with PHI.[33] Such tests, however, do not distinguish between thrombotic encephalomalacia, embolic encephalomalacia or parenchymatous hemorrhage, although the values tend to be higher when there has been hemorrhagic diathesis into the cerebrospinal fluid.

Birth Injury

In a recent survey by Lending and associates[21] GOT and LD levels were determined in the cerebrospinal fluid of newborn infants. The average GOT activity was significantly higher than normal in those infants believed to have sustained paranatal intracranial injury. Cerebrospinal fluid LD activity was even more strikingly elevated. Many of the infants in this group were described as apneic at birth and required vigorous resuscitative measures. Reflexes were often depressed or abolished, and tremors, respiratory difficulty and cyanosis were variably reported. In most of these cases the infants recovered after a few days of supportive therapy. The authors have initiated follow-up studies on the surviving infants. The emergence of sequelae such as cerebral palsy, mental retardation, epilepsy and certain behavioral disturbances may eventually be correlated with increased cerebrospinal fluid GOT activity observed in the neonatal period.

SPHINGOLIPIDOSES

Diseases constituting this group are characterized by a progressive accumulation of metabolically-variant substances (sphingolipids) within the cytoplasm of neurons. The abnormal intracellular storage probably reflects a genetically determined enzyme defect, although the precise catalytic anomalies have not yet been delineated. These infantile and juvenile diseases are unique in that they implicate all neurons, even those of the peripheral autonomic system.

Problems of recognition or nosologic separation do not generally arise with these disorders. The infantile form of amaurotic idiocy (Tay-Sachs disease) is a clearly defined entity with a clinical onset in the first year of life characterized by regression of motor development, hyperacusis and amaurosis. Ophthalmoscopic revelation of cherry-red spots in the macular region confirms the diagnosis. In cases of infantile Niemann-Pick disease with involvement of the nervous system a macular degeneration is seen indistinguishable from that noted in infantile amaurotic family idiocy, but the existence of hepatosplenomegaly in Niemann-Pick disease serves as a clear point of distinction.

Infantile Amaurotic Family Idiocy

Extensive serial enzyme determinations in serum and cerebrospinal fluid have been reported.[2, 3] GOT activity in both biologic fluids is strikingly elevated at inauguration of the disease (four to seven months of life) and gradually regresses, occasionally reaching the normal range if the afflicted child survives more than three to four years. Concomitant assays of cerebral tissue GOT levels show a parallel depression.[4] Since the highest levels of cerebrospinal fluid GOT are found at the beginning of the disease, it may be presumed that liberation of this enzyme precedes neurocytolysis, for the ganglionic destruction is not outstanding until later in the evolution of the disturbance. It is important to note that enzyme elevations may even predate the unfolding of the characteristic neurologic syndrome, and be found at a time when the infant appears to be clinically unaffected.[4] Serum and cerebrospinal fluid LD and MD (malic dehydrogenase) also show a sustained elevation in this disease. The LD levels in both fluids are high in the early months of the disorder, become even higher in the second year of disease and then gradually decline to normal. The elevations of serum aldolase, noted in the second year of illness, have been attributed to the secondary muscle atrophy.

This disease is confined largely to infants of Hebraic ancestry, and studies were instituted to determine whether ethnic background influenced the degree of fluid enzyme abnormality. There were no quali-

tative or quantitative differences in the abnormal biochemical findings in afflicted infants of different racial backgrounds.

Niemann-Pick Disease

Studies in this disorder were confined to those infants with nervous system involvement.[2, 3, 4] The aldolase and GOT findings were indistinguishable from those recorded in infantile amaurotic family idiocy. In Niemann-Pick disease, however, an elevation of the dehydrogenase enzymes was lacking. It seems probable that the massive demyelination and excessive astrocytosis of cerebral white matter which is found only in infantile amaurotic idiocy may be the source of these increased enzymes, particularly since the LD content of proliferating astrocytes is known to be high.

Juvenile Amaurotic Idiocy

This disorder generally commences during the seventh year of life and slowly progresses with blindness, convulsions, paralysis and intellectual deterioration until death supervenes between the fourteenth and seventeenth years of life. The fundamental pathologic change consists in reasonably widespread sphingolipid storage in the cytoplasm of all neurons.[17] Despite extensive involvement of neurons and adjunct tissues, no enzyme abnormalities have been noted in the cerebrospinal fluid of this disorder. The velocity of neurocytolysis is so retarded when compared to infantile amaurotic family idiocy that it is conceivable that the homeostatic mechanisms for the excretion of excessive circulating enzymes has not been overstressed.

DEGENERATIVE AND DEMYELINATING DISEASES

The diagnostic potentialities of enzyme determination have been applied to isolated examples of these disorders, usually during the late phases of the disease. The selective abiotrophy that exemplifies such illnesses as the cerebellar ataxias and the hereditary choreo-athetoses should not theoretically influence the circulating enzyme levels for reasons noted previously. Curiously, Green and associates[12] noted that the cerebrospinal fluid GOT was significantly *below* normal in a case of Wilson's disease.

There are no concerted enzyme studies of the demyelinating diseases of infancy and childhood (Schilder's disease and variants). Scattered data in chronic cases seem to indicate no changes.

Studies by Houck[13] of cerebrospinal fluid ribonuclease may offer some promise in the biochemical identification of these illnesses. This

investigator noted that ribonuclease was normally more concentrated in white matter than gray matter, as opposed to the transaminases, dehydrogenases, cholinesterases and glycolytic enzymes in which the distribution is reversed. Houck applied this test to a limited number of patients with multiple sclerosis and recorded significant rises in all cases, except in those patients in remission. At first glance the diagnostic value of this finding appears to be vitiated by the knowledge that cerebrospinal fluid ribonuclease elevations can be provoked by cerebral infarction, intracranial neoplasms and leptomeningeal infections. These latter lesions, however, also cause elevations of one or more of the previously discussed enzymes (GOT, LD, PHI, aldolase), while the demyelinating disorders apparently do not. On this basis it is possible that the cerebrospinal fluid ribonuclease procedure may be a sensitive indicator of acute demyelination when interpreted in conjunction with other enzymatic parameters.

EPILEPSY

When prolonged convulsions are experimentally induced in young animals, a rapid rise in cerebrospinal fluid GOT and LD ensues. Since these seizures are unassociated with any demonstrable tissue lysis, Lending and her associates[20] proposed that the enzyme release was the consequence of a transient alteration in cerebral cell membrane permeability. The postconvulsive rise in GOT and LD often has not been confirmed in human patients, possibly because the determinations were not performed in the immediately postictal period. Miyazaki[23] was able to demonstrate cerebrospinal fluid GOT increases during or immediately after seizures only.[23] The highest cerebrospinal fluid enzyme values were obtained during status epilepticus in a patient who later succumbed. It would be difficult, of course, to divorce the direct effect of seizures from those of the provocative lesion (e.g. cerebral neoplasm) which independently may contribute to an increase in enzyme liberation.

After electric shock therapy in human beings some observers have noted that the cerebrospinal fluid contained substances capable of degrading chemically pure nucleic acids.[31] These agents were thermolabile and inactivated by magnesium salts, a fact which suggests their enzymic nature. Cerebrospinal fluid GOT is moderately elevated immediately after electric shock therapy.[23] Chapman and Wolff[8] also uncovered a poorly defined proteolytic substance in cerebrospinal fluid after convulsive seizures.[8] Moreover, they also noted the presence of this agent in young schizophrenics and in patients with prolonged migrainous headache. This substance when incubated with plasma proteins initiated smooth muscle contractions.

NEUROMUSCULAR DISEASES

The enzymes mediating glycolysis are impressively concentrated in striated muscle.[9] LD and GOT activity in skeletal muscle is equaled or exceeded only by myocardial and hepatic tissues. Traumatic disruption of muscle in laboratory animals or human beings provokes a sharp but nonsustained rise in serum aldolase, GOT and LD (and, presumably, other enzymes).[38] Extensive skeletal muscle atrophy, on the other hand, is not mirrored by any detectable serum enzyme change, particularly when the atrophy is occasioned by cachexia or immobilization.

Progressive Muscular Dystrophy

In 1949 Sibley and Lehninger[29] noted an elevated serum level of aldolase in two patients with this disorder. Subsequent surveys by Dreyfus, Schapira and Schapira[10] and others have added considerable data supporting this observation.[1, 11, 30, 33, 38] The most dramatic elevations of aldolase (fivefold to tenfold) are found in the childhood (Duchenne) form of dystrophy. The presence or absence of clinically manifest pseudohypertrophy of muscle does not influence the extent of hyperaldolasemia. High levels of aldolase at the onset portend a rapid evolution of the dystrophic process and indicate a poorer prognosis. In the protracted phase of the disease, coexistent with severe muscle wasting, immobility and contractures, the serum aldolase is often normal or subnormal.[1, 28] This may represent an exhaustion phenomenon, since the muscle tissue content of aldolase is inappreciable in terminal muscular dystrophy. A substantial decrease in tissue phosphorylase has also been noted in muscle biopsy specimens from patients with muscular dystrophy.[1, 10]

Since hypoxemia favors the efflux of cellular enzymes, Dreyfus and associates[11] have considered altered muscle cell permeability a possible cause of the hyperaldolasemia associated with muscular dystrophy. Their data suggest that the oxygen consumption in vivo of dystrophic muscle is diminished. Zierler[42] has demonstrated that aldolase leaks from murine dystrophic muscle at a greatly increased rate.

Serum PHI, LD, GOT and GPT (glutamic pyruvic transaminase) display abnormally increased activity, but with less regularity than the aldolase alterations.[10, 11, 25, 27, 33, 38, 41] In the adult type of muscular dystrophy, as well as in myotonic dystrophy, serum enzyme levels are normal or but slightly raised.

Tissue enzyme determinations in experimental forms of muscular dystrophy reveal certain dichotomies which may eventually be applicable to the disease in human beings. White[38] has shown that LD and aldolase activity is depressed, while ICD activity is elevated in muscle

derived from mice afflicted with hereditary muscular dystrophy. Although there is not complete agreement, the muscle tissue aldolase is reported to be increased in murine dystrophy secondary to vitamin E deficiency. In both forms of experimental myopathy the serum aldolase is elevated.[37, 38]

Progressive Muscular Atrophy

The diseases of this group are characterized by a continuing degeneration of spinal cord anterior horn neurons with secondary muscle atrophy and include such clinical entities as Werdnig-Hoffmann disease. A modest rise in serum aldolase has been seen occasionally in these childhood diseases, particularly at the onset of the disease. The elevation is not as striking as in childhood muscular dystrophy.[1] The findings appear inconsistent with the previously cited observation that extensive muscle wasting does not alter serum aldolase. It is possible, however, that the muscle atrophy induced by disease of the lower motor neuron complex differs metabolically from the atrophy secondary to inactivity, diffuse systemic disease or paralysis of cerebral origin. Neurotomy in experimental animals results in a prompt decline of aldolase and succinic dehydrogenase content within the affected muscle and a brief rise in serum enzyme levels.[1, 14]

Myositis

The serum aldolase activity is increased in dermatomyositis, and often impressively so when the disease is severe and generalized.[38] Serum levels of GOT and PHI follow a parallel trend. White[38] has demonstrated that serum aldolase levels may be an accurate representation of the severity of the myositis and an objective measurement of the efficacy of therapy.

COMMENT

The broadening diagnostic contributions offered by enzyme determinations should not be accepted without fully recognizing their present limitations. The magnitude of enzyme activity indicates only the contemporary velocity of tissue degradation and cannot serve to denote the existence of previous tissue damage. In some instances there is a lack of reciprocal correlation between loss of tissue enzyme and elevation of enzyme in biologic fluids, indicating that mechanisms not yet determined govern enzymic interchange.

Additional investigation will be required to lessen the nonspecificity of these biologic tests. Several promising channels have been suggested.

Circulating enzyme is not freely distributed in serum, but rather is linked to certain protein fractions. Electrophoretic separation may offer a technique for the further refinement of enzymologic analysis. It is conceivable that the enzymes may assume characteristic protein-linkage patterns in diseases which otherwise present quantitatively similar serum or cerebrospinal fluid elevations.

Vesell and Bearn[35] have fractionated serum LD into three major components and have proposed that these enzyme components represent distinct types of LD, contributed to the general circulation by different tissues. They noted that the serum LD increase was differentially expressed in the alpha-1 globulin fraction after myocardial infarction, while in leukemia the serum LD rise was largely confined to the alpha-2 globulin moiety.[34] Preliminary studies by Dreyfus and co-workers[11] also suggest that serum aldolase may not be a unitary substance, but rather a number of closely allied but structurally distinct catalytic agents, each derived from different tissues.[11] These investigators considered the possibility that "muscle" aldolase may have a different biochemical action than "liver" aldolase, and hence be potentially separable by critically refined procedures.

Similarly, the intracellular distribution of enzymes is not homogeneous. Some enzymes are principally or exclusively situated within cytoplasmic mitochondria (e.g. alkaline phosphatase, desoxyribonuclease, cytochrome oxidase, ICD), within microsomes (e.g. cholinesterases) or as soluble substances within the cytoplasmic supernatant (e.g. aldolase, LD).[9] Parenthetically, it is interesting that those enzymes intimately associated with a particular metabolic cycle, such as the glycolytic sequence, are present in the same intracellular region. Some of the discrepancies in enzyme release (e.g. elevated serum LD and normal serum ICD in muscular dystrophy) may be accounted for by selective involvement of intracytoplasmic structures. Simultaneous use of a battery of enzymatic analyses may help to delineate those disturbances in which total necrosis of tissue, and hence indiscriminate outpouring of all contained enzymes, is not paramount.

In any consideration of neurologic diseases of infancy and childhood it is pertinent to mention one further potential use of enzyme analysis. A portion of nervous system disorders is clearly of hereditary transmission and presumably attributable to a focal, genetically determined enzyme defect. Inaugural studies in some of the hereditary disturbances of somatic tissues, such as glycogen storage disease, have succeeded in isolating the biocatalytic abnormality and demonstrating it in the biologic fluids. Mommaerts and associates[24] have recently studied a functional disorder of skeletal muscle characterized by a virtual absence of phosphorylase in biopsied specimens. It is probably that the enzymatic aberrations fundamental to the muscular dystrophies, nervous

system abiotrophies, leukodystrophies and sphingolipidoses will be similarly determined in the future.

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NEUROSURGERY IN INFANTS AND CHILDREN

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DIAGNOSTIC SURGICAL CONSIDERATIONS

All diagnostic procedures involving penetration of the body by needles and cannulas (venesection, spinal puncture, ventriculography, angiography, subdural tap, and so on) should be carried out under scrupulous aseptic technique in order to minimize local and generalized infections.

Subdural and Ventricular Punctures. It is essential that the infant be well restrained. After shaving, cleansing and preparing the overlying scalp the lateral recess of the anterior fontanel is punctured obliquely with a pediatric spinal puncture needle. The needle is then slowly but firmly advanced through the dura mater into the subdural space. The stylet is withdrawn. Normally no fluid is obtained from this space. In the presence of a subdural hematoma, bloody xanthochromic fluid drips from the needle. Bilateral puncture should be routinely performed.

Ventricular punctures are similarly carried out through the lateral recesses of the anterior fontanel, the pediatric spinal needle being inserted in the envisioned direction of the anterior horns of the lateral ventricles. When the ventricle is punctured, the stylet is withdrawn and cerebrospinal fluid promptly appears.

Ventriculography is accomplished in the infant through percutaneous transfontanel ventricular puncture and in older children through posterior parietal burr holes. After measurement of the intraventricular pressure the ventricular fluid is exchanged for air in 10-cc. fractions. The ventricles are drained and filled with air *as completely* as possible. In widely dilated ventricles small amounts of air (50 to 100 cc.) not infre-

quently fail to reveal a pathologic process that would readily be revealed by "complete" replacement of fluid by air. At the end of the fluid-air exchange 1 or 2 cc. of indigo carmine may be introduced into the ventricles. Demonstration of the presence (or absence) of the dye in the cerebrospinal fluid obtained through lumbar puncture is helpful in deciding whether a communicating or noncommunicating circumstance prevails between the ventricles and the spinal subarachnoid space. The following views of the skull should be obtained in order to visualize fully the ventricular and subarachnoid systems: anteroposterior (A-P), posteroanterior (P-A), right and left lateral stereoscopic, brow-up lateral, brow-down lateral and "hanging head" positions.

After completion of the ventriculograms the air may be replaced by warm sterile Ringer's solution or by the just-removed ventricular fluid. On occasion, fluid and electrolyte replacement may prove necessary.

SPINAL PUNCTURE AND PNEUMOENCEPHALOGRAPHY are most easily done with the patient in a sitting position. During local procaine (0.5 per cent) anesthesia the lower lumbar subarachnoid space is entered with a pediatric spinal needle. If the infant is not straining, the cerebrospinal fluid pressure should be measured, since it carries positive and negative diagnostic implications. In performing pneumoencephalography *all obtainable* cerebrospinal fluid is replaced by air in 10-cc. fractions. The same roentgenologic views are obtained as those designated for ventriculography. Light general anesthesia facilitates implementation of the procedure in children under 8 to 10 years of age and in uncooperative older children.

MYELOGRAPHY likewise usually necessitates a general anesthetic. A radiopaque medium (2 to 3 cc. of Diodrast) is introduced into the lumbar subarachnoid space with the child in prone position. After fluoroscopic examination of the movements of the medium within the spinal canal suitable roentgenographic films are obtained and the medium is removed through the same needle.

ANGIOGRAPHY requires general anesthesia. In infants and small children the common carotid artery is surgically exposed, and in those beyond the fifth year percutaneous penetration of the artery is accomplished. Three to 5 cc of a radiopaque medium (50 per cent Hypaque) are injected through a no. 18 or 20 Cournand needle into the carotid stream. Several injections may be necessary, depending on the suspected pathologic process, the various head positions desired and whether or not stereoscopic views are required. We regularly obtain films in the anteroposterior, mentovertical and lateral stereoscopic positions during both the arterial and venous phases of circulation of the radiopaque medium.

Vertebral angiography is obtained through injection of the radiopaque medium into the surgically exposed brachial artery.

Anesthesia. The type of anesthesia selected in a given case depends upon the age and size of the infant and the contemplated surgical procedure. Small infants up to the age of four weeks may be easily managed with a sugar-alcohol nipple narcosis, supplemented by local anesthesia. Longer procedures necessitate endotracheal (T tube) intubation. The agents usually used include nitrous oxide-oxygen, supplemented with fluothane, trichoroethylene and sometimes pentothal. Adequate ventilation during anesthesia is essential. The apparatus should not permit rebreathing of carbon dioxide. Depending on the size of the infant and the anesthetic agent, the usual preoperative medication consists of scopolamine and, sometimes, barbiturates. The dosage is proportional to the size of the child.

During the course of operation the heart action is ascertained through a stethoscope strapped over the cardiac apex and a telechor (transistorized amplifier), which makes the heart potentials audible. Intravenous fluids are administered during the course of all operations in carefully measured quantities through the surgically exposed saphenous vein at the ankle. Blood loss is carefully replaced, transfusion being started early during the course of (or even before) the operative procedure.

Local anesthesia is used in all procedures to reduce the amount of inhalation agents required.

Postoperatively the child is placed in a croupette. Inhalation of oxygen and/or steam (cooled or warmed, depending on the child's body temperature) helps to reduce laryngeal edema.

Blood Volume and Blood Loss. The total circulating blood volume at birth is approximately 260 cc., at the age of 3 months 575 cc., and at one year 750 cc. Even small amounts of blood lost during surgical procedures must be promptly replaced in infants.

TRAUMA

CRANIOCEREBRAL TRAUMA

Over-all Prognostic Statistics. The odds greatly favor the physician, for in large, unselected series of head-injured patients some 70 per cent recover regardless of the nature of the treatment (even if negligent) and the time at which it is instituted. Another 9 to 12 per cent die from the overwhelming nature of the cerebral insult, regardless of the expertness of treatment and the promptness of its institution. This leaves a remainder of about 18 per cent—the aggregate of moderately to severely injured but recoverable patients—in whom the particular therapeutic measures adopted and the time of their institution make for greater or lesser degrees of mortality and morbidity. It is to these cases that attention should be directed.

Only about 4 per cent of unselected cases of head-injured patients can actually profit from surgical measures. The majority of patients get

along well on conservative measures alone, and the few that require surgical investigation can be readily identified by the use of certain simple, empirical criteria to be described below.

Management

The clinician confronted with a patient suffering from a moderate to severe degree of head injury will do well to use some generalized, tactical scheme of management such as the following:

1. Perform a brief preliminary examination.
2. Institute first-aid measures as indicated, including those against actual or threatened asphyxiation, hemorrhage, shock and infection.
3. Perform a more thorough examination, both general and neurologic. *Record the findings.*
4. Transport the patient if necessary, "log-fashion" and in the Schaefer position (on the abdomen, head rotated slightly to one side), to a place where all facilities for proper management are available.
5. Complete the examination, using laboratory and other special measures as indicated, e.g. blood cell counts, hemoglobin determinations, blood grouping, serochemistry, urine analysis, cerebrospinal fluid studies, x-rays, and so forth.
6. Institute conservative measures (see below).
7. Examine vital signs (color, pulse rate, respiration, blood pressure and rectal temperature), state of responsiveness ("consciousness") and neurologic status at time intervals appropriate to the severity and changing nature of the clinical picture (e.g. every 15 to 20 minutes up to an hour or two). *Record the findings.*
8. When indicated, implement surgical measures for further diagnostic (ventriculography, cerebral angiography) or therapeutic measures (tracheotomy; débridement, suturing and drainage of wounds; immobilization of fractures of jaws, limbs and ribs; and indicated cranial and intracranial procedures).
9. Resume conservative measures (see p. 547).

Items 6 and 8 call for some elaboration. The others are largely self-explanatory, provided certain special precautions are entertained, as follows:

The presence of marks of violence on the scalp and face does not per se imply that craniocerebral trauma is the sole or even the most serious circumstance responsible for the patient's clinical picture.

The absence of marks of violence on the face and scalp does not per se preclude the existence of serious cranial and intracranial trauma.

Marks of violence on the midforehead or nose should immediately arouse suspicion of a fracture or dislocation of the cervical spine.

If shock is present or impending, its treatment takes precedence over

all other measures. In the brain-injured child shock may, of course, kill within a few minutes of injury. In practice, however, by the time he can be reached by or brought under the care of a physician, he will almost always have recovered in whole or part from shock, provided it is imputable to brain trauma *alone*. If, therefore, the child continues in shock or becomes "shocky" after coming under the physician's care, a careful search for its origin *elsewhere than in the brain* should be instituted (e.g. fractures of long bones, vertebrae and ribs; lacerations of hollow and solid viscera in the abdomen or chest, active hemorrhage [hidden or manifest], peritoneal irritation, exposure to cold, drugs, infection and toxins).

Two measures commonly used to offset shock, namely, narcotics, "to alleviate pain and calm the patient," and lowering of the head, "to improve cerebral circulation," are strongly contraindicated in the head-injured patient.

A lateral horizontal posture is preferable to the "head-down" position. Otherwise measures to combat shock, such as external heat, intravenous fluids, electrolytes, blood, plasma and plasma-expanders, vasoconstrictors and the avoidance of jarring, may be instituted.

Conservative Measures. An *ADEQUATE AIRWAY* must not only be achieved at the outset, but also must be continuously maintained. Merely adjusting the bodily posture so as to facilitate the gravitation of blood, mucus, vomitus and the tongue away from the hypopharynx often suffices. An oropharyngeal airway, with or without oxygen (6 to 7 liters per minute), is helpful. Repeated aspiration of the nasopharynx and oropharynx and the tracheobronchial tree, "fishing" skilfully for mucus, is often necessary. If, despite these simple measures, mechanical interference with respiration persists, early use of a tracheostomy tube is indicated. Regular cleansing of the oropharyngeal and tracheostomy tubes is essential. Humidifying devices are highly desirable in treating infants and children.

Posture. If the patient is not "shocky," he should be placed on a soft mattress, the bed being set as for a low Fowler's position (head end 15 to 20 degrees above horizontal). Unless a tracheostomy tube is already in place, he should be placed fully over on one side and his position changed, slowly, deliberately and in "log-fashion," to the opposite side every two hours to prevent hypostatic pulmonary congestion and decubitus ulcers.

Restlessness. If not excessive, restiveness is desirable rather than the reverse. Side rails, well padded, will usually be necessary to prevent self-injury. Unless the limbs are restrained by padded elbow splints and/or wrist and ankle cuffs, the patient may imperil his dressings, wounds, nasal and bladder catheters and nasogastric tube. Camisoles ("straight jackets") are occasionally required.

If it appears necessary to control restiveness, chloral hydrate and sodium bromide, with or without paraldehyde, are distinctly preferable to narcotics and barbiturates. They may be given singly or combined, by mouth, nasogastric tube or rectum (in milk), in doses appropriate to age and weight.

Although temporary incontinence of the bladder and rectum is the rule in patients rendered stuporous by head injury, retention of urine with resultant bladder distention sometimes occurs and incites considerable restlessness. Gratifying amelioration can be obtained by the use of an indwelling catheter for a few days.

Fever. Uncontrolled, hyperthermia can, by itself, prove lethal. Whenever the rectal temperature exceeds 102.5° F., complete stripping of the body and continuous sponging of the limbs and trunk with a half-and-half mixture of tepid water and alcohol are indicated. Lowering the room temperature to between 55 and 60° renders the procedure more facile. Aspirin administered every three to four hours by mouth or nasogastric tube is a useful adjunct.

Antithermic measures must be continued until the rectal temperature falls to about 101.5° F. and promptly resumed whenever the fever again exceeds 102.5° F. If these devices prove insufficient, the physician may resort to *repeated* colonic instillations of cool tap water, the amounts ranging from a pint to 1 or 2 quarts, depending on the size of the patient. After being warmed in the colon for about five minutes the water should be siphoned off and the process repeated. Before initiating such measures an "axillary equivalent" of the rectal temperature should be determined to guide the conduct of this modality of antithermic treatment.

Fluids, Food and Electrolytes. Early passage of a nasogastric tube is extremely helpful in the endeavor to provide needed fluids, electrolytes, nourishment and medications. An excellent "balance" can usually be achieved for weeks on end by allowing 50 to 100 cc. of fluid to gravitate into the stomach every hour, rotating among 5 per cent glucose water, strained fruit juices and eggnog.

Orificial Bleeding and Cerebrospinal Fluid Discharge. Bleeding from the nose or ear, with or without cerebrospinal fluid "leak," need not excite undue alarm. In most cases cerebrospinal fluid discharge ceases spontaneously within a few hours to days. Surgical intervention is not necessary during the acute phase.

The involved orifice may be gently swabbed as occasion demands, but packing, irrigating and instilling medicaments are strongly contraindicated. Broad-spectrum antibiotics (ideally, those to which the offending bacteria have been shown sensitive) should be administered.

Convulsions. Children are prone to exhibit *focal* and/or *generalized tonic-clonic seizures* after even mild cerebral injuries. Such seizures do not necessarily augur ill for the future.

Once under way, the average, sporadically occurring seizure cannot be stopped, nor need special efforts be made to stop it. The patient should be protected against self-injury and asphyxiation. Often-repeated seizures, on the other hand, demand active anticonvulsant measures (e.g. barbiturates by mouth, muscle or vein, bromides and/or hydantoinates by mouth, and, in stubborn cases, Avertin by rectum and/or ether by inhalation).

Tonic seizures (as opposed to clonic focal and general) suggest the possibility of surgically amenable epidural or subdural clots in the posterior fossa. More often, however, they signify "decerebrate" or "decorticate" phenomena and are indicative of interstitial hemorrhages extravasated within the brain stem or of widespread damage to and swelling of the cortical and subjacent hemispheral structures. Although grave, these signs do not necessarily presage a fatal outcome. Drugs are of trivial therapeutic value for tonic seizures, but ample ventilation of the brain, with or without oxygen therapy, must be provided. With modern methods of treatment over 65 per cent of children with decerebrate seizures may be expected to survive. Complete psychologic and neurologic recovery is not infrequently achieved by persistent treatment.

Elimination. Incontinence of urine and stool is common. Excreta should be cleaned way from the skin, diaper and bedclothes as soon as they appear. An indwelling bladder catheter with a simple clamp saves much soiling and permits intermittent emptying and flushing of the bladder with antiseptic agents (50 to 100 cc. of 0.25 per cent acetic acid alternating with aqueous Zephiran chloride, 1:20,000). Constipation is rarely a problem. If it presents, glycerin suppositories and saline enemas may be used.

General Measures. As in the management of all seriously ill patients, routine nonspecific and hygienic measures appropriate to good general nursing care (e.g. of the mouth and so on) are essential.

SURGERY. Compound fractures of the vault, whether linear, stellate or comminuted, with or without depression and with or without indriven bony fragments, call for conveniently early (though not necessarily immediate) operation. So also do "simple," closed, depressed fractures of the vault (whether "Ping-Pong ball," "pond," "gutter," "button" or "stellate" in type) whenever the outer table of the depressed portion is at or below the level of the inner table of the nondepressed portion. Cerebrospinal fluid leaks suggest the need to take skull x-rays to determine whether an intracerebral pneumocele of the frontal lobe exists. This condition calls for early relief, lest a brain abscess develop at the site of the air pocket. The dural rent at the base of the skull should be patched with a fascial autograft.

Preliminary x-rays of the skull (anteroposterior, posteroanterior and right and left laterals) are helpful in planning all operative procedures

and in any case should be obtained with a view to their possible medicolegal use.

The indications for operation in the three conditions referred to above are clear-cut. With regard to the remaining types of surgically amenable lesions—epidural, subdural and intracerebral clots and lobar pulpification—the indications are not nearly so clear-cut, for the clinical pictures corresponding to these pathologic processes are especially ambiguous in children.

The one most reliable indication of the need for surgical investigation is that, despite faithful exercise of conservative measures, the patient begins and continues to "lose ground." Such loss of ground is betrayed by (*a*) persistent drifts of vital signs in any direction away from normal ranges and/or frequent fluctuations ("instability") from time to time within normal and near-normal ranges, (*b*) increasing stupor, and (*c*) progressive neurologic dysfunction (pupillary disparities, conjugate deviation of the eyes, motor and sensory pareses and paralyses, incoordination and reflex disparities, vomiting, and so on). When such signs present, biparietal burr holes and direct inspection for epidural or subdural hematomas must be implemented. Eighty per cent of such clots will be revealed by this simple procedure. If no clots are apparent and if the brain appears swollen, ventriculography should be immediately performed. In recent years increasing reliance has been placed upon cerebral angiography. Neither ventriculography nor angiography is infallible. Nevertheless, *demonstration of a shift or other distortion of the normal ventricular system or of the normal cerebrovascular pattern makes surgical investigation mandatory.* Multiple lesions may be thus suggested. In any case, the surgeon deals as judiciously and definitively as possible with each lesion.

After operation the conservative regimen previously outlined is to be resumed.

CHRONIC SUBDURAL HEMATOMA, HYGROMA AND HEMOHYGROMA

These conditions are usually, though not invariably, initiated by trauma. The injury may have occurred from a week or more to several months before the appearance of overt clinical manifestations and may have been relatively slight, yet sufficient to disrupt the fragile veins of the hemispheral surface and the arachnoid membrane. The veins that "bridge" from the cortex to the dural sinuses at the vertex and base of the skull appear to be especially vulnerable.

Clinical Signs and Symptoms

In infants and young children whose cranial sutures, if closed, remain relatively loose, the classic syndrome of chronic subdural hematoma as

seen in the adult (essentially that of increasing general intracranial pressure) is not closely simulated. Convulsive seizures constitute the most common feature of the clinical picture. Focal sensory, motor and coordinative dysfunctions are rare. The nonspecific signs of poor feeding, failing nutrition, periods of irritability and restiveness interlarded with periods of apathy and lethargy, low-grade fever, vomiting and crying aloud as if from bouts of pain (and, in the articulate child, complaints of generalized headache) constitute by far the most common manifestations. Papilledema is uncommon, but may be present with or without retinal hemorrhages. The advent of visible enlargement of the cranium in consequence of progressive "external hydrocephalus" may be the first indication that the responsible etiologic factor lies within the head. Internal strabismus, indicative of abducens nerve palsy, carries a general, rather than focal, significance.

Lumbar puncture is a nondiscriminating test, although a finding of xanthochromic cerebrospinal fluid (necessarily a "contaminant" of the subarachnoid space) suggests that a subdural hematoma or hemohygroma *may* coexist. Far more conclusive in differential diagnosis are parasagittal bilateral transdural taps. Such taps are feasible, of course, only in infants in whom firm closure of the sutures and fontanel has not yet occurred. Bilateral lesions are present in about half the cases, though not necessarily of equal magnitude. A greater volume of subdural fluid can be tolerated when distributed fairly equally on both sides than can be tolerated alone or mainly on one side.

Treatment

Daily removal by transdural taps of a total of 10 to 15 cc. of subdural fluid if necessary, over the course of several days, is recommended. In bilateral cases the daily taps should alternate from one side to the other. The fluid removed may range in color from deep cherry red to pale yellow.

Subsidence of abnormal clinical signs is frequently apparent from the beginning of treatment, and successive taps commonly reveal diminishing xanthochromia and shrinking volume of the fluid drawn off until the taps give trivial yields. Unfortunately, the tapping process in some cases inadvertently precipitates new bleeding.

If, on a regimen as outlined above, improvement comes to a halt short of full complement, or if, despite the taps, the patient continues to do poorly and the head size increases inordinately, craniotomy with resection of the capsular membrane and its contents should be performed. If bilateral operation is required, some one to two weeks should elapse between the first and second stages.

The majority of children do well when this general strategy is used.

Patients who for any reason are not given the benefit of such management frequently exhibit progressive blindness and other neurologic and psychologic decrements, convulsive phenomena, progressive hydrocephalus, herniations of the temporal lobe and cerebellar tonsils, stupor and grave states of malnutrition. If brain stem hemorrhages or ischemia ensues, death occurs.

In some cases the brain is so severely subjected to molding ("plastic creep") by the subdural mass that "re-expansion" after surgical evacuation of the subdural mass takes place sluggishly, if at all, and incompletely. The space between the brain and dura then continues, despite repeated taps, to refill with a mixture of fresh and old blood and cerebrospinal fluid. A sort of "stalemate" develops between the dynamics of the lesion and the therapist's efforts. The condition carries a guarded prognosis. In such cases a "shunt" type of drainage is indicated (see p. 566).

By and large, the prognosis is favorable for recovery if the subdural clot is detected before neurologic and intellectual defects supervene.

TRAUMA TO THE SPINE AND SPINAL CORD

Incidence

In large part because of the suppleness of young tissues, trauma to the spine and spinal cord is less frequently encountered in infants and children than in the adult, the ratio being about 1:12.

Principal Sites of Damage

The more mobile portions of the spinal column, namely, the cervical and lumbar regions, are involved much more often than the thoracic and sacral portions. Moreover, they are more frequently attended by damage to the spinal cord and cauda equina.

It should be borne in mind that spinal trauma may coexist with other injuries, including craniocerebral. Frontal craniofacial trauma should prompt investigation for cervical spine injuries.

Pathologic Types of Bony Damage

Falls (including dives) and falling objects, in which the physical force impinges mainly upon head, shoulders or buttocks, commonly result in transient "jackknifing" deformations of the spinal axis and wedge-shaped compression fractures of the vertebral bodies, with or without corresponding damage to the intervertebral disks. The more violent insults produce, in addition, vertebral fracture-dislocations, with severe disruptions of the spinal ligaments, displacements (anterior, posterior

or lateral) of that portion of the spinal axis above the level of injury with reference to that below, and shearing damage to the pedicles and articulating facets. Such injuries are almost always of "closed" type.

Direct insults to the spine (e.g. by missiles, baseball bats and heavy vehicles) are more likely than the indirect to produce "open" wounds and to damage the dorsal and transverse processes, laminae or facets, as opposed to the vertebral bodies.

Pathologic Types of Spinal Cord Damage

By no means all instances of demonstrable vertebral column damage in children result in spinal cord damage. The ratio approximates 5:1. On the other hand, grave spinal cord damage occasionally presents without demonstrable clinical and x-ray evidence of vertebral column injury.

By far the commonest pathologic process in the indirectly traumatized spinal cord consists in multiple, interstitial, often confluent, petechial hemorrhages within the substance of the cord (hematomyelia). Such lesions are most obvious in the gray matter, but are found also in the white matter. The most conspicuous changes are at the cord level of greatest vertebral damage, but they may extend superiorly and inferiorly in serpentine fashion for as many as six or more cord segments. Intramedullary swelling and edema usually superadd to the hemorrhagic elements. The spinal subarachnoid space may thus be compromised and blocked off.

Injuries by picks, knives, bullets and, occasionally, crushing objects may lacerate or contuse the cord, either directly by themselves or by displacing bony structures which impinge upon it. Anatomic transection is rarely met with in civilian practice.

Paraspinal injuries (e.g. high-velocity missiles) sometimes produce multiple disseminated tissue disruptions and cavitations within the spinal cord. Such may or may not be attended by interstitial hemorrhagic elements. These acute lesions are not infrequently distributed widely over many cord segments. Ultimately they are resolved as gliosis, vacuolization and status spongiosus. Here, as in hematomyelia, some greater or lesser degrees of enduring parenchymatous changes with corresponding functional deficits are to be expected.

Clinical Manifestations

VERTEBRAL. Pain is usually severe at the outset and should always prompt a local examination. Swelling, contusions and laceration of the skin and underlying soft tissues will often be at once apparent, though their absence does not preclude vertebral damage. In the young child with a "closed" injury, local deformities of the spinal column (angular

kyphosis, scoliosis, rotation and subluxation) are often directly visible and even more often palpable. In any case, x-ray films of the vertebral column and rib cage should be obtained early. *Negative x-ray findings do not exclude an initial transient, vertebral body dislocation with "spontaneous" reposition.* Such instances are easily prone to redislocation, sometimes with disastrous effect.

THE SPINAL CORD AND ITS ROOTS, INCLUDING THE CAUDA EQUINA. Greater or lesser degrees of sensory and motor paralyses—in the great majority of cases bilateral—are apparent fom the moment of injury on. Delayed paralyses (30 minutes to 1 or 2 days) may occur, however, much more often in children than in adults. With few exceptions, the sensory deficits are both cutaneous and kinesthetic in type.

Immediately after injury and for varying periods of time thereafter (from a week to three or more months) "spinal shock" prevails in the somatic and visceral structures below the dermatome corresponding to the highest cord segment damaged. In cervical damage, quadriplegia, and in thoracic and lumbar damage, paraplegia, is the rule. Concomitantly, the deep and superficial reflexes are absent. The urine is characteristically retained unless the damage involves the conus medullaris or cauda equina, in which case more or less continuous dribbling prevails. Paralytic ileus not infrequently develops during the first week. It is especially prone to appear with "self-arrested" retroperitioneal hemorrhage.

As spinal shock recedes, mass reflexes (transient, diffuse somatic muscle activities attended by "goose flesh" on the skin of the afflicted limbs, dermatographia, micturition and, in high thoracic and cervical injuries, priapism) may appear. The somatic motor phenomena are gradually supplanted by flexor synergic responses to noxious stimuli and, later, by extensor synergic, "postural" responses to deep tactile stimuli. At such time the familiar "upper motor neuron" signs (hyperreflexia, ankle clonus, spasticity, Babinski and Babinski-confirmatory signs) gradually appear in the lower limbs in those instances in which the traumatic lesions lie above the uppermost lumbar cord segments. Lesions situated at lower lumbar and sacral segments result in "lower motor neuron signs" (flaccid, atonic, areflexic state of the lower limbs). It is, of course, possible to have "lower motor neuron signs" in the upper limbs and "upper motor neuron signs" in the lower limbs.

Thereafter recovery may be *complete* or nearly so in the sensory and/or motor-coordinative realms. More often, however, it is *partial* (to varying degrees) or *nil*. During the period of recovery from cord trauma, motor power usually returns earliest in the more peripheral members of the limbs (toes, fingers, feet and hands) and only later, if at all, in the appendicular muscles attached to the shoulder and pelvic girdles. Improvement is not usually to be expected beyond the thirtieth month.

Conservative Measures of Management

In cord trauma, as elsewhere, the treatment or prevention of *shock* takes precedence over all other matters demanding attention.

Pain and *restlessness* may be controlled by local, soft tissue injections of procaine hydrochloride (1 per cent) or by narcotics and barbiturates given parenterally or by mouth. In high or midcervical injuries (in which respiratory compromise of diaphragmatic and intercostal muscles is present or imminent) local injections of procaine are to be preferred. Narcotics and barbiturates may irreversibly imperil an already damaged but adequately functioning neurorespiratory apparatus.

If needed, *transportation* should be accomplished by moving the patient gently, firmly and quickly in "log-fashion." Cervical injuries call for a moderate dorsal extension of the head, long axis traction being simultaneously exerted on the head with countertraction on the feet. Such a maneuver is most easily accomplished during transportation by applying the hands under the chin and occiput. A split, 5-inch wide muslin bandage achieves similar ends and is somewhat less tiring on attendants.

The cervically injured patient should be transported in the supine position. Lateral movements of the head should be prevented by appropriate padding. Those with injuries to the thoracic and lumbar levels may be transported, again in log-fashion, in such a way as to accomplish a mild to moderate dorsal extension of the spine. If a sagging litter is used, the patient should be carried in the prone position; but if the litter is taut, the patient should be carried supine, a rolled up blanket or similar pad being placed snugly under the spine to accentuate the lumbar physiologic curve.

The cervically injured patient often depends wholly upon diaphragmatic breathing. Early, at least, he is continually in jeopardy from compromise or loss of the remaining phrenicorespiratory mechanism. The various measures for combating threatened asphyxiation (suction apparatus via nasal catheter, oxygen therapy, oropharyngeal airway, emergency tracheotomy, face mask with inflatable breathing bag, automatic "bubble" type of pump-respirator and modern "iron lung" type of respirator) should be available for instant use.

Sustained treatment of the cord-injured patient consists of general nursing, hygienic and nutritive measures appropriate to all seriously ill patients plus use of certain devices for preventing those complications that most frequently result in morbidity and death, namely, *hypostatic pulmonary stasis* and *pneumonitis, decubitus ulcers* and *bladder infection*. In this connection the following regimen will be found helpful:

1. Use an air or fluted automatic massaging (Gardner) mattress.
2. Turn the patient (log-fashion), alternating from side to back and

from back to opposite side at two-hourly intervals. Massage "pressure areas" after each turning. Protect persistently reddened areas with "doughnut" pads.

3. Insert an indwelling bladder catheter and institute tidal type of drainage from the outset. Use mild antiseptic solutions.

4. Give broad-spectrum antibiotics and sulfonamides by mouth and/or parenterally.

5. Clean all excreta promptly from bedclothes and skin.

6. As soon as tolerable to the patient, passively exercise all paralysed members through full range of motion at each joint at least thrice daily.

Surgical Measures

Neurosurgical procedures have relatively limited role in injuries of the spine and spinal cord.

It is, of course, mandatory to débride thoroughly all "open" wounds and remove devitalized tissues, pieces of clothing and other foreign bodies that might foster the development of meningitis, abscess and septicemia. In such cases prophylactic and therapeutic doses of antibiotics are strongly indicated. Surgical drainage may or may not be necessary.

Fractures and dislocations of the cervical spine can usually be comfortably reduced and maintained by using traction by tongs (e.g. Crutchfield's), the tips of which are inserted bilaterally through the outer table of the parietal bones. A rope attached to the tong-arch at the midline passes over a Buck type of extension pulley and supports a weight (appropriate to the size of the child) of 3 to 8 pounds. While in such traction, the patient can be moved with impunity from back to side and nursing measures can be readily implemented.

Cervical fractures that cannot be reduced within two to three days by tong traction are unlikely to be reduced with longer continued or heavier traction, principally because the facets have "locked." Such a circumstance calls for closed manipulation and reduction during general anesthesia by the "Taylor maneuver" (passive flexion or extension of the patient's head, as indicated by the radiologically demonstrated deformity; unlocking of the facets; exerting of strong linear traction; and reposition of the dislocated vertebrae along the longitudinal axis of the spine).

If no neurologic damage prevails in the form of dermatomal analgesia and anesthesia involving the neck, shoulders and upper portion of the trunk, a Minerva type of plaster of Paris cast may be applied at any convenient time after achievement of closed reduction and kept in place for six to eight months. In the presence of sensory deficiencies, however, plaster of Paris immobilization is distinctly contraindicated,

because it threatens decubitus ulceration. In such case skull traction should be used for six weeks and then discontinued. Thereafter the head should be passively moved, as needed, for changes in the patient's posture, and splinted in position with external, padded supports for some three to four months. Meanwhile the upright position should be interdicted unless an adjustable stiff, padded plastic or felt surgical collar is used.

Severe compression fractures and dislocations of the lumbar spine, whether "open" or "closed," can be readily reduced during general anesthesia by "slinging" the prone patient between two tables, the trunk being free and in moderate dorsal extension. Traction and countertraction are steadily exerted by two assistants at the axillae and ankles. The operator now imposes a steady, downward push with his fist against the kyphotic site until reduction is accomplished. A plaster of Paris body cast, holding the spine in slight to moderate extension, should then be applied.

Fractures of the odontoid process should be dealt with by "open reduction," as far as possible, and by immobilizing the first and second cervical joints by autologous bilateral rib grafts, laced by wire to the denuded bony cortices of the laminae, from the occiput to and including the fourth cervical vertebra. No Minerva cast is required after such grafting. The patient can be allowed to sit up and stand within a day or two of operation.

Fractures of the vertebral dorsal and transverse processes require no reduction. Pain is considerable in such cases, but fortunately can be managed by local procaine injection.

By and large, surgery has dubious therapeutic value in cases of spinal cord injury. The parenchymatous damage imposed at the time of trauma is not likely to be favorably alterable by laminectomy, decompression or removal of laminar fragments or facets displaced to the spinal canal, for hematomyelia, cavitation, and intrinsic swelling of the cord are not surgically amenable lesions.

Some surgeons regularly undertake laminectomy if a "block" of cerebrospinal fluid can be demonstrated by the Queckenstedt test. Others deny that this is a useful criterion. There may, however, be some diagnostic merit in direct surgical inspection of the site of damage, even if definitive therapeutic measures cannot be implemented. For in those cases in which the cord is severely lacerated or pulpified, the prognosis as to what may be anticipated by awaiting "spontaneous" recovery for a year or more can be quickly settled and realistic plans made for rehabilitation and ambulation. There may also accrue to parents and patient the psychologic advantage inherent in the overt conviction that "no stone was left unturned." Such advantages may offset in part the risks involved in operation.

Persistent, well circumscribed root pains may be readily handled by dorsal rhizotomy. Diffuse burning types of pain and aching, and dysesthesias and paresthesias in the portions of the body below the level of injury can often be relieved by excision of the cicatrized and gliotic proximal spinal cord or by bilateral anterolateral chordotomy.

Bothersome flexor spasms of the lower limbs, painful or not, foster the development of "sheet burns" and decubitus ulcers. The spasms can be alleviated either by anterior rhizotomy of the first lumbar to the second sacral roots inclusive, or in the completely and permanently paraplegic subject, by cordectomy of the lumbosacral enlargement.

Young patients suffering from the flaccid "lower motor neuron" type of paraplegia can usually be taught to ambulate by using suitable long or short leg braces with crutches (later, with canes). The spastic, "upper motor neuron" type of paraplegia, however, may need to be surgically converted into the flaccid type by anterior rhizotomy or cordectomy. This is especially likely if the patient is subject to unpredictable flexor spasms of the lower limbs and trunk.

Rehabilitation, education and vocational training should be started as early as possible with a view to preventing development of habits of overdependency and self-commiseration within the patient.

TRAUMA TO THE PERIPHERAL NERVES

Incidence and Types

In the newborn, facial nerve and "brachial plexus" injuries (e.g. Erb's type of palsy) constitute the principal types of peripheral nerve injury. Many instances clinically regarded as involving the brachial plexus constitute, in fact, avulsions of the spinal nerve roots from the cervical cord.

Older children are susceptible to all the usual types of peripheral nerve and plexus injuries encountered in adults—excessive traction, lacerations, contusions, intrinsic hemorrhages and scarring, extrinsic impingements by bone, foreign bodies and scars. Washing machine wringer injuries are common.

Clinical Manifestations

Pain is usually absent or inconspicuous. For this reason the physician's attention is not readily invited to the nerves of the affected part, especially when concomitant injuries (e.g. soft tissue and vascular lacerations and fractures of long bones) engage him. *To avoid errors of omission, therefore, a deliberate search for signs of peripheral nerve damage must be regularly undertaken.*

Sensory, reflex and *motor deficits* constitute the three important realms to be explored. The presence of dysfunction in one or more of

them can be quickly ascertained by the use of pinpoint, reflex hammer and appropriate (verbal or demonstrative) directions to move each of the innervated members distal to the site of injury. The particulars of examination will, of course, vary with the member(s) under inquiry.

Treatment

Débridement and thorough inspection are required of all "open" wounds. If the paralyzed nerves (e.g. median, radial, ulnar and sciatic) are found at operation to be in continuity, they should be left alone. But if they are found interrupted, neurorrhaphy should, if possible, be done *at this time*, even in the face of potential sepsis.

In the presence of "closed" wounds the clinical demonstration of preservation of *any* sensorimotor functions regularly mediated by the nerve under inquiry suggests that anatomic continuity, at least in part, prevails. Such a finding warrants expectant treatment. It does not, of course, exclude an anatomic interruption in cases harboring atypical innervations (e.g. in which "typical" ulnar nerve functions are mediated by the median nerve, and vice versa).

Even with clinical evidence of *complete* sensorimotor paralysis of the nerve under inquiry, temporization is in order in "closed" cases for six to nine weeks. Functional tests should be performed at least every 10 days. If increasing functional return, however slow, is noted, temporization may be justified; but if no functional return is observed after two months, or if functions present from the outset or those subsequently regained show a decrement, surgical exploration is indicated. Neurolysis (freeing the nerve from surrounding scar, bony callus or impinging bone) may be all that is indicated; or neurorrhaphy (trimming, freshening and suturing the ends of the interrupted nerve) may be necessary. To accomplish repair of extensive gaps may require transposition of the nerve. A plaster of Paris cast or other immobilizing splint, with or without a turnbuckle for gradual control of limb extension, must be used for four to six weeks after neurorrhaphy.

Interruption of the elements of the brachial plexus is seldom surgically reparable because of the limited mobilization of its components that can be effected. The chief exceptions to this statement are those relatively rare cases in which soft tissue scars or bands extrinsic to the cords can be freed up.

Physical therapy should in all cases be instituted from the outset, starting well before and being resumed soon after operation.

If early recognized and attacked before irreversible facial muscular fibrosis develops, severe facial nerve palsy of the newborn due to forceps compression can sometimes be effectively dealt with by direct operation, seeking identification of damaged branches of the seventh nerve

behind or within the parotid gland. An electronic stimulator is useful in distinguishing between viable and nonviable nerve elements. Wherever indicated, neurolysis and/or neurorrhaphy should be performed, these measures being generally more rewarding than abandonment of treatment. The prognosis for complete recovery is not optimistic, but some improvement is generally to be expected.

In mild to moderately severe cases of facial nerve paresis, whether due to trauma, otitis media, mastoiditis or surgical accident, operative treatment is insufficiently rewarding to be justified. In the more serious cases, anastomoses with the spinal accessory, hypoglossal or phrenic nerves are helpful, provided they are made within three months of injury. Thereafter fibrosis of the distal segment of the facialis nerve or the muscles it innervates seriously compromises surgical benefit.

CENTRAL NERVOUS SYSTEM ANOMALIES

The causes of anomalies involving the neural axis and the supporting mesodermal tissues that form bone, cartilage, fat, blood vessels, meninges and connective tissue are unknown. Such congenital defects probably arise during the first few weeks of embryonic development.

SPINA BIFIDA; MENINGOCELE; MYELOMENINGOCELE

Spina bifida results from an incomplete fusion of one or more laminae of the vertebral column and may be accompanied by protrusion of the spinal cord or its membranes through the vertebral defect.

In *spina bifida occulta* there is no extrusion of intraspinal contents. This anomaly is usually asymptomatic, but may on occasion be accompanied by a cutaneous defect (dimple, sinus, hypertrichosis) or by subcutaneous lipomas. Musculoskeletal, sensory defects and sphincteric disturbances are uncommon. Unless one or more of these objective findings suggests the presence of spina bifida occulta, the diagnosis is made by roentgenography only (see below).

Meningocele constitutes the relatively rare herniation of dura mater and arachnoid (alone) beyond the spinal canal and through the subcutaneous tissue and deep layers of skin overlying a spina bifida. More commonly, anomalous neural and glial elements of the spinal cord and nerve roots accompany these membranes into the herniated sac. Such constitute a *myelomeningocele*. These lesions may occur at any level of the spinal axis, but most frequently in the lumbosacral area. Depending on the location of the defect and the extent of neural involvement, the patient may present various degrees of paralysis, sensory loss and sphincteric disturbances. In lumbosacral lesions flaccid paralysis and loss of sensation in the lower extremities (sometimes resulting in contractures

or dislocation of the hips and foot deformities) are common. They are usually accompanied by paralysis of the rectal and vesical sphincters with resulting incontinence and local skin maceration. Frequently associated with these lesions are other central nervous system malformations (e.g. hydrocephalus) and extraneural anomalies of the genitourinary and skeletal systems and heart. Hernias are also likely to be present.

Treatment

The indications for and timing of surgical treatment of meningocele, myelomeningocele and symptomatic spina bifida vary from clinic to clinic. In any case, operative treatment aims at removal of the protruding mass so as to facilitate nursing care of paraparetic infants and prevent infection. Neurologic improvement is not to be expected. Operation in the early postnatal period is rarely necessary, but may be performed in uninfected, small simple meningoceles in infants exhibiting no apparent neurologic deficit. The removal of broad-based myelomeningoceles must often be delayed until enough surrounding skin is available for closure of the defect. Repair of leaking, ulcerated or frequently infected lesions must be deferred until the infection is controlled and ulceration healed. The potential development or actual progressive coexistence of hydrocephalus should not be considered a contraindication to repair of a myelomeningocele, though when present, it may demand prior consideration and treatment.

The unoperated sac should be protected from trauma, rupture and ensuing infection by keeping the infant on the abdomen. The sac should be surrounded by a doughnut-shaped ring of cotton or foam rubber and kept scrupulously clean. Its surface can be washed daily with boric or acetic acid solution and, if necessary, covered with an antibiotic ointment. Preoperatively, the lesion, and immediately postoperatively, the surgical wound must be carefully protected from contamination with urine and feces by sealing off from the excretory orifices with a plastic sheet.

CRANIAL MENINGOCELES AND ENCEPHALOMENINGOCELES

These occur most frequently in the occipital region, and may vary greatly in size. They may contain meninges, cerebrospinal fluid, cerebral tissue and even parts of the ventricular system. Except when large amounts of nonfunctioning brain tissue are present in the encephalocele, or when the hernia is complicated by hydrocephalus, the neurologic deficit is not conspicuous.

In general, early operation is recommended to prevent ulceration, rupture and infection and to facilitate nursing care. The prognosis for life and function is generally more favorable than that of analogous spinal lesions.

CRANIAL AND SPINAL DERMAL SINUSES

Sinus tracts extending from the surface of the skin to the skull, vertebrae, meninges, brain or spinal cord may exist at any point along the posterior axial line, from the skull to the caudal region of the spinal column. Most frequently they occur in the lumbosacral and occipital areas. Most of these consist of epithelial-lined tracts which end blindly in the meninges and are asymptomatic. When infected, they may give rise to meningitis and any of the complications thereof. Occasionally the tracts are connected to dermoid cysts which, because of their size and location, may give rise to the symptoms and signs characteristic of intracranial or intraspinal tumors. Intracranial and intraspinal dermoid cysts are discussed in the sections on intracranial tumors, pages 689 to 698, and intraspinal tumors, pages 568 to 569.

Roentgenograms often reveal a small, discoid defect in the skull and/or a spina bifida occulta, close to the opening of the dermal sinus.

Treatment consists in excision of the tract to prevent infection. This should be performed early in life.

DIASTEMATOMYELIA

This consists of a congenital malformation in which the spinal cord is divided longitudinally into two portions by a bony, cartilaginous or fibrous septum arising from the anterior aspect of the spinal canal. The anomaly is most common in the lower thoracic and upper lumbar regions. The septum divides the neural canal partially or completely for a distance of one to several segments in the anteroposterior axis and thus transfixes the spinal cord. The cord is thus immobilized at the involved level and cannot "ascend" in the neural canal with longitudinal growth of the vertebral column. As the vertebral column lengthens, traction is exerted on the fixed cord. A progressive neurologic deficit, especially of the lower extremities, commonly ensues.

Patients regularly present localized hypertrichosis in the midline of the back, usually covering the region of the underlying spinal anomaly. Often associated with such hairy tufts are congenital dermal sinus, lipoma and skin dimple. Neurologic disturbances include impaired function of one or both lower extremities with weakness, muscular atrophy, reflex and sensory changes. Impairment of rectal and bladder functions and low back pain occasionally develop. Although the cutaneous and bony anomalies are present at birth, the neurologic disorders may not become evident until the patient starts to walk.

The *diagnosis* of diastematomyelia and its exact location depends upon radiologic and myelographic determinations. Spina bifida occulta with associated fusiform widening of the spinal canal and other ver-

tebral anomalies are regularly present. Myelography outlines the characteristic midline bony cartilaginous or fibrous septum.

Treatment consists in exposure of the defect through a laminectomy, removal of the midline fibrous cartilaginous or bony septum and mobilization of the split spinal cord. Occasionally, section of a taut filum terminale is also necessary.

CRANIOSYNOSTOSIS

Premature closure of various cranial sutures is characterized by anomalies in the shape of the skull. The most common of such disorders results from premature fusion of the sagittal suture. It is characterized by an elongated, narrow skull and is rarely associated with other anomalies or neurologic symptoms. Unilateral or bilateral coronal synostosis produces a high, broad and short skull and is frequently associated with exophthalmos, facial dysostosis and hypertelorism. Other anomalies include persistent opening of the metopic frontal suture, *Lückenschädel*, myelomeningocele and congenital heart disease. Premature fusion of several suture lines may occur. When craniosynostosis is combined with syndactylism and acrocephaly, it is called Apert's disease. In some cases craniosynostosis associated with severe craniofacial dysostosis appears to depend upon hereditary factors (Crouzon's disease).

Neurologic disturbances include visual loss, papilledema, optic atrophy, extraocular muscle disorders, anosmia, hearing deficiencies, convulsions and mental retardation. Secondary obstructive hydrocephalus may develop. Although the anomalous shape of the skull is noticeable at or soon after birth, neurologic disorders may not become evident until after the first year of life. The clinical diagnosis of premature synostosis of cranial sutures is confirmable by radiologic examination.

Treatment consists in removal of the cranial periosteum and performance of linear craniectomies which act as artificial suture lines during the period of maximal growth of the brain. Orbital decompression may be necessary in cases of exophthalmos with visual loss. The best cosmetic results are obtained in patients with sagittal synostosis when operated upon before the age of four months. In general, early operation is recommended.

HYDROCEPHALUS

Hydrocephalus ("internal hydrocephalus") is an abnormal, progressive accumulation of cerebrospinal fluid within the ventricular system producing distention of the cerebral ventricles. It is not synonymous with enlargement of the head, which may increase in size while the ventricular system remains normal in size, as may be the case in tumors

and subdural hematomas and effusions. In older children the cranial sutures are closed, and hydrocephalus does not increase the size of the head; in babies, however, the hydrocephalus separates the cranial bones, and the skull may assume large proportions. Hydrocephalus results from an obstruction somewhere along the cerebrospinal fluid pathways. For clinical purposes it may be divided into *noncommunicating* and *communicating* hydrocephalus.

Noncommunicating hydrocephalus is characterized by a blockage along the ventricular system interfering with communication of this system with the subarachnoid space. The cause of obstruction may be (1) congenital malformation, (2) inflammatory and postinflammatory reactions, and (3) neoplasm.

Congenital malformations may include stenosis or malformation of the interventricular foramina, producing dilatation of the lateral ventricles alone; of the aqueduct of Sylvius, causing dilatation of the lateral and the third ventricles; and atresia of the foramina of Magendie and Luschka, resulting in a generalized hydrocephalus including enlargement of the fourth ventricle. This last condition is usually associated with agenesis of the cerebellar vermis.

Hydrocephalus is frequently associated with spina bifida and meningocele or myelomeningocele and may be obstructive as a result of an Arnold-Chiari malformation (see p. 567). It is less frequently met in association with cranial meningocele or encephalocele.

Inflammatory reactions (endothelial and fibroblastic proliferative) resulting from infection, trauma or hemorrhage may likewise produce obliteration of the subarachnoid spaces and cisterns. Ventriculitic adhesions can form and obliterate the interventricular foramina, the third ventricle, the aqueduct of Sylvius and the exits of the fourth ventricle. Obstructive hydrocephalus secondary to bacterial meningitis is not infrequent. The arachnoid becomes solidly plastered against the foramina of Magendie and Luschka. Similar reactions may take place in the arachnoid over the entire brain, more commonly at the base of the brain and around the spinal cord, preventing the cerebrospinal fluid from reaching the subarachnoid space over the hemispheres, where it is normally absorbed.

Intracranial tumors may mechanically obstruct any part of the cerebrospinal fluid pathways, directly or indirectly. They sometimes invade the ventricular system itself. In children, noncommunicating hydrocephalus is frequently caused by cerebellar or "fourth ventricle" tumors (astrocytoma, medulloblastoma), tumors invading or compressing the third ventricle (pinealoma, craniopharyngioma) and large temporal lobe gliomas compressing the aqueduct. In many instances of unsuspected tumor the initial symptoms are produced by the noncommunicating hydrocephalus.

In *communicating hydrocephalus* satisfactory communication obtains between the dilated ventricular system and the lumbar subarachnoid space. The obstruction is located in the subarachnoid cisterns at the base of the brain or along the subarachnoid spaces over the surface of the brain itself, impairing absorption of the cerebrospinal fluid. Obstruction of the subarachnoid cisterns around the brain stem and over the base of the brain is a frequent sequel of meningitis, especially of the tuberculous variety. Hypersecretion of cerebrospinal fluid by choroid plexus or choroid plexus papilloma is also said to be a cause of communicating hydrocephalus.

Diagnosis

Differentiation between noncommunicating and communicating hydrocephalus can usually be made by a dye test or by ventriculography.

The dye test consists in injection of 1 or 2 cc. of indigo carmine into one lateral ventricle. The dye diffuses rapidly through the cerebrospinal fluid. Unless a block occurs at the interventricular foramen, portions of it mixed with cerebrospinal fluid may be obtained within a few seconds by puncture of the opposite ventricle. Lumbar puncture performed 20 or 30 minutes after injection of the dye reveals, in the presence of a noncommunicating hydrocephalus, clear cerebrospinal fluid. In the presence of communicating hydrocephalus the fluid is stained blue.

Ventriculography, performed by puncturing the lateral ventricles through the lateral recesses of the anterior fontanel or through bilateral burr holes in the posterior parietal regions and replacing the ventricular fluid by air, is a more accurate diagnostic procedure than the dye test. It is important to replace as much of the ventricular fluid by air as possible in order to obtain adequate filling of the ventricular system (see p. 543). This procedure permits evaluation of the size of the hydrocephalus and visualization of the site of obstruction. Adequate filling of the third ventricle, aqueduct and fourth ventricle and cervical subarachnoid space is necessary to determine the presence of a communicating hydrocephalus. In the presence of lesions producing noncommunicating hydrocephalus the air does not travel beyond the site of obstruction.

Partial obstruction is revealed in ventriculograms by dilatation of the ventricular system above the lesion and small, often incompletely filled cerebrospinal fluid pathways, below the lesion. Such may be encountered in third and fourth ventricular tumors and in neoplasms of the brain stem.

Treatment

For centuries the treatment of hydrocephalus has consisted in drainage of the ventricles or the lumbar subarachnoid space. Many mechanical

methods of external and internal drainage have been devised. All methods have been at least temporarily successful, but all have had many failures and complications. Successful surgical alteration of the pathophysiologic process is regularly possible only if the obstruction is caused by a tumor which is accessible and completely removable or by a congenital or postinflammatory membrane at the outlets of the fourth ventricle and/or the cisterna magna which can be opened and excised. Unfortunately the majority of infants and children do not fit into these groups and must be treated by other methods.

Most of the shunting procedures are done with single or multiple rubber, plastic or silicone tubes. Complications are frequent. With the growth of patients the tubes become disconnected or pull out of their intended location. The tubes themselves are prone to become obstructed, kinked or broken. They may produce tissue necrosis. When placed within blood vessels, they tend to produce thrombosis. Accumulation of draining cerebrospinal fluid in body cavities may produce reactions which stop absorption. Infection is common and is the more serious because of the presence of a foreign body leading to cerebrospinal fluid pathways. When connected with the nasopharyngeal cavity or the urinary tracts, shunting tubes form an ideal path for ascending infections.

The following procedures have had a limited measure of success in the treatment of obstructive hydrocephalus:

Choroid plexectomy consists in transcortical coagulation or excision of parts of the choroid plexus in the lateral ventricles. It is a procedure of choice in hydranencephaly, since it allows direct inspection of the intracranial anomaly and thus helps in formulating a prognosis.

Third *ventriculostomy* consists in puncture of the lamina terminalis and the floor of the third ventricle and may be performed when for any reason direct inspection of the chiasmatic or pituitary region is deemed desirable.

Ventriculocisternostomy (*Torkildsen procedure*) involves introduction of a tube into one lateral ventricle and shunting of the cerebrospinal fluid around the obstruction in the ventricular system into the cisterna magna or, preferably, the cervical subarachnoid space. This is the procedure of choice when exploration of the posterior fossa seems indicated or when a known ventricular obstruction (e.g. thalamic tumor) cannot be directly removed.

Ventriculocisternostomy (*Hyndman procedure*) is produced by removal of the glomus of the choroid plexus at the time of choroid plexectomy in one lateral ventricle, thus producing an opening into the cisterna ambiens.

Ventriculomastoidostomy consists in shunting the ventricular fluid through a tube into the antrum or a large mastoid cell.

Ventriculocaval shunt involves insertion of a tube into a lateral ventricle from which the cerebrospinal fluid may be delivered into the superior vena cava or the right atrium by way of the internal jugular vein. A one-way valve system prevents reflux of blood into the ventricle. Complications are frequent, but relatively easy to remedy.

Ventriculoperitoneal shunt uses a long tube to connect the lateral ventricle to the peritoneal cavity. It is of value in cases of hydrocephalus associated with paraplegia and sphincter paralysis.

Ventriculoureteral shunt involves leading the ventricular fluid through a long tube into one ureter. Removal of one kidney is, of course, required. It is contraindicated in the presence of bladder anomalies and infections of the kidney and urinary tracts. Excreted electrolytes need daily replacement.

Ventriculofallopian tube shunt consists of a tube leading from a lateral ventricle into one fallopian tube. The latter must be ligated close to the uterus. The cerebrospinal fluid leaks from the fimbrial end of the fallopian tube into the peritoneal cavity, where it is absorbed.

Ventriculojejunal shunt connects the ventricular system with an isolated loop of jejunum.

Ventriculopleural shunt leads the ventricular fluid into the pleural space for absorption.

In the treatment of communicating hydrocephalus some success has been obtained with shunts which connect the lumbar subarachnoid space to (1) the peritoneal cavity, (2) a ureter, (3) a fallopian tube, and (4) a loop of jejunum. Ventriculomastoid and ventriculocaval shunts are also useful in cases of communicating hydrocephalus.

In more than 250 cases of hydrocephalus treated in our clinic, revisions after shunts were necessary in 95 instances. Approximately 100 are functioning satisfactorily. Eighty patients died of complications (meningitis, ventriculitis, septicemia, superior vena cava thrombosis, and others) or of increasing intracranial pathology. Because of failures, many cases were treated with several types of shunts.

ARNOLD-CHIARI MALFORMATION

This consists in a herniation and compression of parts of the cerebellum, fourth ventricle, medulla oblongata and pons into the upper cervical canal. It is frequently associated with myelomeningocele, malformation of the aqueduct of Sylvius, obstructive hydrocephalus and bony defects in the region of the foramen magnum and the upper cervical spine.

In addition to the symptoms caused by hydrocephalus and myelomeningocele, patients with this malformation have nuchal rigidity, retraction of the head and severe pain on flexion of the head. They may die suddenly of acute respiratory failure.

Treatment consists in suboccipital and upper cervical decompression and surgical treatment of the hydrocephalus. The results have been disappointing. Though often suspected on clinical grounds, the condition is usually diagnosed at autopsy.

INTRASPINAL TUMORS

Although relatively rare in children, intraspinal tumors (see also p. 698) occur at all ages and at all spinal levels. They consist of primary intramedullary gliomas (e.g. astrocytoma and ependymoma); secondary intramedullary and extramedullary gliomas (seeding from intracranial medulloblastoma, pinealoma, astrocytoma); intradural extramedullary dermoids, neuroblastomas, ganglioneuromas, meningiomas, neurofibromas and arachnoid cysts; and extradural teratomas, sarcomas, chondromas, giant cell tumors of the bone and osteoidosteomas. Ruptured intervertebral disks are occasionally encountered in older children.

Diagnosis

The symptoms arise gradually, and early at least, little attention is given them by parents. Backache may be absent, especially with intramedullary tumors, but is perhaps the most common and persistent symptom. It is often attributed to mild injuries sustained during rough play, laziness, and so on. As the pain gradually increases it may interfere with the child's playing, running and walking and eventually force him to remain immobilized in bed. Coughing, sneezing, bowel movements and other Valsalva-like acts which raise the intraspinal pressure or put traction upon nerve roots commonly augment the pain. Pain-alleviating postures (spinal lordosis, kyphosis and scoliosis) often coexist with the pain. Awkwardness of motion exhibited by the child when rising, sitting, bending and squatting invites suspicion of a spinal pathologic process. Sensory disturbances and deficient control of the sphincters are often difficult to evaluate in small children and infants, but in those over five or six years of age they are as significant as in the adult. Postural deformities of the extremities with muscle weakness and atrophy are not infrequent. Exaggeration of or diminution in the tendon reflexes and the presence or absence of the Babinski sign and its "confirmatories" are similarly significant of lower and upper motor neuron damage. Skin anomalies (sinus, dimple, hypertrichosis) suggest the presence of a dermoid or teratoid tumor.

Given such clinical manifestations, the identification and localization of spinal tumors depend largely upon cerebrospinal fluid findings, roentgenograms and myelograms. When tumor is present, lumbar puncture performed under sedation may reveal evidence of partial or complete

subarachnoid block (positive Queckenstedt test) and yellow cerebrospinal fluid with an increased protein content. Whenever a spinal lesion is suspected, roentgenograms of the entire spine should be made. Vertebral anomalies may be associated with dermoids, teratomas and arachnoid cysts. Widening of the spinal canal, thinning of the pedicles and concavity of the posterior surface of the vertebral bodies are often caused by expanding intramedullary or extramedullary tumors. Destruction of vertebral components and extraspinal soft tissue shadows are often seen with sarcomas and extradural vertebral ("dumbbell") neurofibromatous tumors.

Pantopaque myelography performed under general anesthesia localizes fairly accurately the level of the tumor and supports the clinical diagnosis of spinal tumor.

Treatment

Laminectomy and surgical excision of intraspinal tumors should be instituted as soon as the tumor is accurately localized. Most benign tumors can be completely removed. When malignancy involving the vertebrae is encountered, surgical efforts are limited to decompressing the spinal cord and nerve roots. Such lesions may later be treated by roentgen therapy. If well circumscribed, intramedullary gliomas and ependymomas can be completely excised. Associated cysts may be opened and drained. Extensive infiltrative gliomas, however, can rarely be removed. Surgical measures then consist of bony decompression followed by roentgen therapy.

Extensive laminectomies or irradiation in growing children is occasionally followed by skeletal deformities (e.g. kyphosis, lordosis and scoliosis). Youngsters so treated may need plaster jackets or braces to prevent or correct these deformities.

Physiotherapy and re-education in the use of the extremities are extremely important if paraparesis, paraplegia or loss of proprioception is present in the extremities. These measures should be instituted as soon as possible after operation. Postoperative disability in control of the bladder and bowel functions recovers relatively easily in children and rarely leads to serious complications.

INFECTIOUS PROCESSES

BRAIN ABSCESS

Etiology and Pathology

Intracerebral abscesses in children are established in descending order of frequency by the following mechanisms:

Hematogenous—from any focus of infection in the body (mouth,

lungs, heart valves, and so forth). The offending microorganisms may be of virtually any coccal or bacillary variety. When sepsis of the mouth is the source, mixed infections, including fungi, are not unusual.

Direct extension—from infections of the paranasal sinuses, middle ear, mastoid cells, and elsewhere. Intermediary pathologic processes usually consist of adjacent osteitis or osteomyelitis, retrograde thrombophlebitis and a transient, relatively circumscribed meningitis. By far the commonest microorganism here is the pneumococcus.

Penetrating and *perforating craniocerebral wounds*, with or without foreign bodies. As with the hematogenous mechanism, almost any pathogenic microorganism may be the offender.

A *complication* of the acute *meningitides*. Influenzal, pneumococcal, meningococcal and staphylococcal organisms constitute the principal offenders.

Pathogenesis

The pathophysiologic disturbances fall into two main classes.

General disturbances are due to increasing intracranial tension and to compromise of the circulation of blood or cerebrospinal fluid and independent of the locus of the abscess.

The clinical manifestations consequent upon such changes include progressive headaches, nausea, vomiting, bradycardia, blurred vision, periodic restiveness and lethargy, intellectual blunting, confusion, indifferent control of sphincters and psychotic symptoms. In the infant, enlargement of the skull, and in the older child, papilledema (with or without retinal hemorrhages) eventually occur. Deepening stupor and coma may be, but are not necessarily, attended by arterial hypertension and stertorous breathing with Cheyne-Stokes cycles.

Unilateral or bilateral abducens nerve palsy, resulting in internal strabismus and diplopia, more commonly arises from general rather than focal compromise of intracranial dynamics. The Gradenigo syndrome (which is consequent upon extension of middle ear or mastoid disease to the petrous tip and in which local osteitis compromises the abducens nerve and fibers of the ophthalmologic division of the fifth nerve) represents a notable exception.

Focal disturbances (due to local ischemia, toxic effects, mechanical pressure and spatial shift of brain tissues) are peculiar to the locus of the abscess.

Lesions confined to "silent areas" of the brain (e.g. frontal lobe or superior parietal lobule) produce only general disturbances as enumerated above, with or without sporadic, grand mal convulsions, whereas those located in or near projection areas produce signs and symptoms as follows: (1) *irritative phenomena* (sensory or motor seizures of jack-

sonian type [without altered states of responsiveness] or other focal types [attended by more or less altered states of responsiveness]), and/or (2) *paralytic phenomena* (monoparesis, hemiparesis, various types of cutaneous and proprioceptive anesthesia, visual field defects, dysphasia, dysarthria, dyspraxia, dysgnosia, and so on).

Abscesses involving the cerebellum are usually unilateral. They commonly produce focal signs in the nature of equilibratory and nonequilibratory incoordination (faulty balance, wide-base gait, ataxic intention movements of trunk and limbs, ipsilateral hypotonus, head tilting, nystagmus characterized by a slow component to the side of involvement, and, on occasion, tonic seizures).

Diagnosis

Differential diagnosis between brain abscess and the conditions most closely simulated by it (brain tumor, chronic subdural and intracerebral hematomas, and progressive cyst formation) may be resolved, provided the historical data and the general clinical findings are favorable. The electroencephalogram may aid in localizing the site of disease, but unfortunately is nondiscriminating. Pneumoencephalography may be used to demonstrate the presence and locus of a space-usurping mass, but carries the risks attendant upon rapid herniation of brain tissue through the tentorial incisura or foramen magnum and cannot be recommended. Cerebral angiography and ventriculography offer comparable information more safely.

Treatment

When brain abscess is strongly suspected, the wise strategy is to *delay operation as long as one is not forced to intervene*. General supportive measures, anticonvulsant and "specific" or broad-spectrum antibotics should be vigorously used. Delay favors the development of a firm capsule and reduction of peripheral swelling of the brain.

Vigilance for loss of neurologic functions, for decline in the state of responsiveness ("consciousness") and for aberrations of the vital signs should be closely exercised. Whenever such decrements appear to become precarious, operation should be performed.

The most satisfactory surgical procedure consists in craniotomy and complete extirpation of the abscess, the surgeon dealing with the abscess as if it were a well circumscribed tumor.

A useful but appreciably more protracted procedure consists in repeated (daily?) aspiration of pus through a large-bore needle. Similarly, drainage of pus may be accomplished by an indwelling, soft rubber tube. In both methods the capsule is intentionally left *in situ*. Early collapse

of the capsule may occur and lead to formation of a "daughter abscess."

Optimally managed, brain abscess carries an over-all mortality rate of between 15 and 20 per cent. Enduring neurologic sequelae appear less commonly in cerebellar than in supratentorial lesions. Among the latter they must be expected in slightly more than half the cases.

OSTEOMYELITIS OF THE CRANIAL VAULT

This condition, essentially a chronic, smoldering infection which involves the diploë more rapidly and extensively than the cortical tables of the skull, may result from direct trauma to the skull, extension of an adjacent soft tissue infection or hematogenous infection. Once established, it may be retarded and delimited by antibiotics, but is only rarely cured by such therapy alone. Infected granulomas tend to proliferate between the affected bone and underlying dura mater. Complications in the form of local or diffuse meningitis and brain abscess are prone to ensue.

Clinical Manifestations

Swelling and tenderness of the soft tissues of the scalp, cervical lymphadenopathy, low-grade fever, leukocytosis and increased sedimentation rate should arouse suspicion, especially if a current or relatively recent "break" in the scalp is recognizable. Skull x-rays often reveal a circumscribed, "moth-eaten" area of the vault. It is rare to obtain free pus by aspiration of the subaponeurotic space overlying the osteomyelitis.

Treatment

This consists of appropriate antibiotics by mouth or parenteral routes; supportive measures (including hematinics or transfusion if anemia is present); *wide* surgical resection of the bone; and drainage until all signs of sepsis have receded.

Osteomyelitis of the base of the skull is not susceptible of surgical attack. Reliance must be placed wholly upon antibiotics and supportive therapy. The prognosis is grave.

POSTMENINGITIC COMPLICATIONS

After favorable recession of the acute and subacute phases of the specific (meningococcal) and nonspecific (staphylococcal, streptococcal, pneumococcal and bacillary) meningitides, two varieties of complications and sequelae may be encountered: *internal hydrocephalus*, due to inter-

ference at one or more crucial sites in circulation of the cerebrospinal fluid, and *subdural effusion.*

The management of postmeningitic internal hydrocephalus, whether "communicative" or "noncommunicative" in type, is essentially that appropriate to the management of internal hydrocephalus of other origins (see p. 565).

Subdural effusions constitute one of the several conditions subsumed by the term "external hydrocephalus." The postmeningitic effusion is characteristically straw-colored, usually somewhat cloudy, and rich in protein content (frequently exceeding 1 or more gm. per 100 ml.). It may be relatively localized or widely spread over the hemispheral convexity. On occasion it extends between the hemispheres. Empyema, sterile or nonsterile, may complicate the effusion.

The clinical manifestations trail after those of the antecedent acute pyogenic meningitis and persist well beyond the time when convalescence should have been achieved. By and large, they resemble the general signs described in connection with subdural hematomas, internal hydrocephalus and brain tumors. The patient usually appears more prostrated, however. Focal signs are usually inconspicuous.

The condition is serious and, if unrecognized or unsuccessfully managed, is prone to prove fatal within several months.

Treatment consists in wide craniectomy, evacuation of the subdural effusion, disruption of all loculations, and external drainage for as long as is required to effect complete resolution. At some later time the defect of the bony vault may be plastically repaired.

SPINAL EPIDURAL PYOGENIC INFECTION

Etiology, Pathology and Pathogenesis

Infection of the epidural fat is occasionally introduced directly. In the vast majority of instances, however, it is hematogenous, derived from a recently past or currently active infection located elsewhere in the body. With few exceptions, the staphylococcus is the offending bacterium. The evidence is strong that vertebral osteomyelitis (often unrecognized clinically, radiologically and at operation) is a regular antecedent of infection of the epidural fat.

The pathologic involvement of the epidural tissues may range through a wide spectrum, characterized by free pus in the more acute, variously circumscribed cellulitic infections in the subacute, and indolent granulomas, superficially resembling Hodgkin's disease, in the chronic pictures. Leptomeningitic reactions, from slight to severe, may be seen in all forms.

The spinal cord may or may not be mechanically compressed by the

epidural lesion. Without regard to this factor, it may suffer serious compromise of its function in virtue of the interference with drainage of its blood by thrombotic and thrombophlebitic processes. In severe cases the resulting intramedullary congestion and ischemia lead to an irreversible "status spongiosus" of the cord.

Clinical Manifestations

In subacute and chronic cases the antecedent infection may have cleared and been forgotten by the patient. The history then given and the relatively slowly advancing neurologic deficits cannot be clinically distinguished from those of extramedullary neoplasms (see p. 568). Pain and tenderness in the back may be relatively slight. Radiologic evidence of osteomyelitis of the centrum, pedicles or laminae of one or more vertebrae is, of course, strongly suggestive of the existence of a subacute or chronic epiduritis. But absence of such radiologic evidence does not exclude the diagnosis.

Because the more acute epidural infections constitute surgical emergencies (in that a few hours may make the difference between complete recovery and enduring paraplegia), special attention should be directed to it. The story is typical and is closely simulated by no other condition: (*a*) antecedent or current infection; (*b*) boring pain lasting from one to several days in the region of and tenderness overlying a vertebra; (*c*) a hyperesthetic dermatome at the level of the involved vertebrae accompanied by root pains that are augmented by coughing, sneezing and straining; (*d*) hyperesthesias, dysesthesias and paresthesias of the skin below the level of spinal cord involvement; (*e*) progressive weakness of the lower limbs; (*f*) loss of sphincteric control; and (*g*) rapidly progressive sensory and motor paralysis, usually of the hypotonic, areflexic type. Lumbar puncture usually reveals a complete subarachnoid block ("positive" Queckenstedt test).

Diagnosis

The x-ray film rarely reveals evidence of osteomyelitis, even though such actually exists. Once suspicion of an epidural abscess is aroused, a no. 18-gauge spinal needle may be cautiously advanced through the dorsal intervertebral ligaments and ligamentum flavum and into the epidural space at the level of greatest tenderness. Retrieval of pus makes the diagnosis. Extreme care should be exercised to avoid perforating the dural and arachnoidal membranes and carrying infection more deeply.

Antibiotic therapy should be promptly instituted and a laminectomy performed, extending from just above the upper to just below the lower limits of the visibly infected epidural fat. The exposed "gutter," con-

sisting of paravertebral muscles and epidural tissues, should be lightly packed with gauze and drained openly until all evidences of purulent discharge subside.

INTRACRANIAL VASCULAR DISORDERS

SPONTANEOUS SUBARACHNOID HEMORRHAGE; INTRACEREBRAL BLEEDING

Spontaneous Subarachnoid Hemorrhages

Among children the commonest cause of nontraumatic extravasation of blood into the subarachnoid space or the cerebral ventricles is rupture of an arterial, venous or arteriovenous angioma. Other causes include acute inflammatory or toxic encephalopathies (including the encephalitides), blood dyscrasias (leukemias, purpuras, sickle cell anemia, and so on), and erosion of a blood vessel within a brain tumor which gives rise to disruptive bleeding beyond the limits of the tumor.

Bleeding into the ventricle cannot be confidently differentiated clinically from that into the subarachnoid space. The former, however, is more likely than the latter to be followed promptly by grave, even fatal, consequences.

Intracerebral Bleeding

Such bleeding, initiated by any of the factors enumerated above, may remain confined to the brain substance, i.e. may not break into the subarachnoid or ventricular spaces. In such case the self-tamponading clot behaves like, and cannot be confidently differentiated on clinical grounds from, any other space-usurping mass (e.g. brain tumor and subdural hematoma).

Nontraumatic intracranial hemorrhage is characterized by a sudden onset of severe headaches, followed promptly by repetitious vomiting, shock and alterations of consciousness ranging from lucidity or a lightly dazed to a comatose state. The commonest neurologic symptoms include nuchal rigidity, positive Kernig's sign and paresis of one or more extraocular muscles. Depending upon the severity and locus of the lesion, monoplegia, hemiparesis, hemianopsia, speech disturbances and focal or generalized convulsions may ensue.

During the first several days the cerebrospinal fluid obtained by lumbar puncture contains frank blood and, when centrifuged, reveals a clear, xanthochromic supernatant fluid. Later the corpuscular elements are lysed, and xanthochromia persists for upwards of two to three weeks.

Blood dyscrasias should be ruled out in all instances. If such studies prove negative, cerebral angiography is in order to help in differential

diagnosis and in localizing the lesion. In children carotid angiography is best done under general anesthesia.

The most frequent cause of subarachnoid hemorrhage in children is rupture of an *arteriovenous malformation* (arteriovenous angioma). This malformation consists of a mass of thin-walled vessels fed by arteries and drained by large veins transporting arterial blood. It may be single or multiple, on or beneath the cortex or connected with the ventricular wall. Large neonatal arteriovenous aneurysmal sacs have been reported between the posterior cerebral artery and the vein of Galen, producing severe hydrocephalus by compression of the aqueduct.

Treatment

Once angiographic localization has been accomplished, ligation of the feeding arteries and extirpation of the lesion should, if possible, be instituted to prevent further (and possibly fatal) hemorrhages. The surrounding intracerebral hematoma and disrupted devitalized brain should also be removed. Anticonvulsant medications for the control of seizures may be needed for months or years after surgical removal of the lesion.

CONGENITAL ARTERIAL ANEURYSM; STURGE-WEBER SYNDROME; INTERNAL CAROTID ARTERY THROMBOSIS

Congenital arterial aneurysms, although present from birth, rupture distinctly less frequently among children than among adults. They may be associated with polycystic kidneys or coarctation of the aorta. Most often they involve the internal carotid artery, at the site of branching of the posterior communicating artery, or near the bifurcation of the anterior and middle cerebral arteries. Here, again, diagnosis depends on carotid arteriography, and treatment consists in ligation of the involved internal carotid artery. If arteriography suggests the presence of a hematoma, craniotomy and evacuation of the clot are indicated. Direct surgical attack on the aneurysm is the procedure of choice.

The *Sturge-Weber syndrome* is characterized by congenital cutaneous angioma ("port-wine stain"), usually in the distribution of one division of the trigeminal nerve. Several years may elapse before additional evidences of the syndrome, e.g. convulsive seizures, spastic hemiparesis and mental deficiency, become apparent. Intracortical and subcortical calcifications may occasionally be suggested by plain roentgenograms of the skull. Cortical telangiectases may be visualized by carotid angiography.

Treatment is directed toward control of the convulsive seizures with Dilantin and phenobarbital or other drugs.

Lobular or lobar resection and, on occasion, hemispherectomy of the subordinate hemisphere have been advocated in cases of uncontrollable convulsions.

Internal carotid artery thrombosis may arise suddenly in children and is characterized by sudden hemiplegia. It may also be associated with hemianopsia and aphasia. Diagnosis is made by carotid arteriography. Treatment is conservative and recovery gradual, usually incomplete.

CEREBRAL PALSY

Neurosurgical measures have a relatively small place in the management of certain types of cerebral palsy. They are applicable to the following conditions:

HYPERKINETIC DISORDERS

These include chorea, athetosis, alternating tremor, dystonic, ballistic and intention types. Such abnormal movements occur in about half of all sufferers from cerebral palsy. They are notably refractory to medical, pharmaceutic, physical therapeutic and psychiatric measures.

The *pathology* and *pathogenesis* of these disorders are but obscurely understood. Thus far it has not been possible to hold damage to any one brain structure responsible for the production of hyperkinesia in general, much less for any one of the special clinical types.

Surgical Measures

At the Level of the Basal Ganglia. The extirpations of motor and premotor cortices and the high cervical, anterolateral and dorsolateral cordotomies advocated during the first half of the current century for alleviation of the hyperkinesias and postural abnormalities of cerebral palsy regularly entailed a serious compromise of sensory, motor and eupractic functions yet remaining to the patient. For this and other reasons they have been largely supplanted by "deep" subcortical operations, in which relatively safe and accessible portions of the nervous system giving origin, transit or terminus to the ansa lenticularis are surgically interrupted. The "target" selected may be the globus pallidus, the ansa lenticularis coursing lateral to the paraventricular hypothalamic nucleus, the dorsal margin of the substantia nigra, Forel's field H_2 or the ventrolateral nucleus of the dorsal thalamus. The techniques of producing such deep-seated lesions—whether by leukotome, electrocoagulation, chemocoagulation, ultrasound or nuclear radiation—regularly involve the use of ventriculography, three-dimensional coordinate maps

of the human brain and a suitable stereotactic device. Electrostimulation may be used to provide supplementary topologic information.

Surgery does not aim at destruction of the pathologic process responsible for the disorder, but at interruption of one (or more) neural structure(s), the integrity of which appears essential to perpetuation of abnormal movements and muscle tonus.

The mortality rate of such operations is about 5 per cent. Failure to achieve and maintain envisioned improvement occurs in about 15 per cent of cases. In addition, there is a risk that functions preserved preoperatively may be partially or completely lost after operation. All risks are perceptibly augmented when bilateral (two-staged) operation is undertaken.

At Midbrain Level. For the more severely afflicted athetotic, dystonic and ballistic patients, in whom quadriparesis, reduced intellect and compromise of speech prevail, abnormal movements and spasmodic rigidity can be largely eliminated and nursing care facilitated by performing unilateral or bilateral (two-staged) midbrain crusotomy. A mortality rate of 5 per cent for unilateral and 10 per cent for bilateral cases must be entertained. Cortisone and Pro-banthine therapy should be used prophylactically preoperatively and postoperatively to counteract postoperative tendencies to fluid and electrolyte imbalance and gastric bleeding.

INFANTILE SPASTIC HEMIPLEGIA

The combination of hemiplegia and repeated convulsive seizures, with or without severe antisocial behavior disorders and with or without intellectual decrement, constitutes a small but medically and psychosocially troublesome group of cerebral-palsied patients. Diffusely atrophic gliotic and cicatricial changes, sometimes attended by intracerebral cyst and porencephalic outpouchings of the ventricles, are confined largely to one hemisphere. The presumption is that, initially, an embolic, thrombotic or disruptive episode involved one or more major cerebral vessels.

Clinical Features

A moderate degree of somatic hemiatrophy involving the facial, truncal and appendicular structures contralateral to the side of cerebral atrophy is common. The hemiparesis is regularly of spastic type with characteristic postural alterations, deep tendon hyperreflexia, upper motor neuron signs and circumduction gait. Dysarthric speech is usually present, but dysphasia is not.

The electroencephalogram reveals "epileptiform" and other dysrhythmias, usually obvious over both hemispheres, but more noticeably over the manifestly damaged side. Pneumoencephalography, ventriculography

and cerebral angiography provide radiologic confirmation of the pathologic changes in the hemisphere.

Seizures may occur as often as 50 to 1000 times per year; may be of any type—minor, major, focal, general or psychomotor—and are relatively refractory to anticonvulsant medication.

Surgical Measures

Subtotal hemispherectomy (sparing the thalamus and hypothalamus) is highly successful in alleviating or abolishing the convulsions and in ameliorating behavioral disorders. The preoperative hemiparesis is not usually worsened, and the hemihypesthesia may or may not be increased. An enduring hemianopsia must be accepted as a sequel of operation.

The operative mortality rate is about 5 to 8 per cent.

The postoperative electroencephalogram as recorded over the opposite hemisphere usually shows a decided improvement, occasionally approaching normal. Similarly, the I.Q. score may be improved up to 50 or more points, presumably in consequence of the recession of restlessness, negativism and distractibility. Postoperative reduction of intake of anticonvulsant drugs and improvement in motivation also appear to contribute to the gains in I.Q.

SPASTICITY

Relatively circumscribed somatic muscle hypertonus, characterized by increased stretch reflexes (tendon hyperreflexia, Babinski and Babinski-confirmatory signs), is productive of much disability in virtue of the postural alterations (talipes equinovarus, adductor "scissoring," and so on) imposed. It results from the play of excessive neural impulses along the alpha (somamotor) and gamma (fusimotor) neurons. Such impulses are produced by corticofugal "upper motor neuron" damage.

Partial relief of spasticity and corresponding clinical improvement can often be obtained by selective neurectomy of the appropriate peripheral nerves (e.g. the motor branches of the tibialis, peroneal or obturator nerves). Likewise, muscle recessions (e.g. of the gastrocnemius), tenotomies and arthroplasties may be used to advantage, either independently of or in conjunction with neurectomy. The risks to life are slight.

Posterior rhizotomy (Foerster's operation) has proved largely disappointing. On the other hand, anterior rhizotomy is of value in properly selected cases (method of Munro). A new operation proposed by Kerr, namely, transverse horizontal myelotomy, promises to be useful in certain cases of spastic diplegia.

INTRACTABLE EPILEPTIC SEIZURES

As exhibited by the cerebral-palsied child, recurrent epileptiform seiz-

ures, whether focal or generalized, pose problems no different in principle from those encountered elsewhere in pediatrics. The pertinent surgical aspects are discussed in the next section.

PAROXYSMAL CONVULSIVE DISORDERS

A comprehensive discussion of the clinical types of epilepsy encountered in infancy and childhood (their incidence, etiology, pertinent pathology and medico-psychologic management) has been prepared by Dr. Millichap (see p. 583). The present section is concerned principally with the surgical management of recurrent convulsive seizures.

It will be assumed that progressive etiopathologic agents (e.g. brain tumors and parasitic cysts) which, whether or not attended by convulsions, require treatment in their own right have been appropriately ruled out. It will likewise be assumed that the patient has had the benefit of a competently implemented course of treatment on the standard anticonvulsant pharmaceuticals, used singly and combined and pushed to tolerance, and that the frequency and severity of seizures nevertheless continue in such manner as to warrant acceptance of the risks, anxieties, inconveniences and costs of operation.

Although helpful in many instances, surgery provides no guarantee that convulsions will be eliminated.

Types of Seizures in Which Operation Has Proved Efficacious

These include jacksonian or other focal, grand mal, grand mal interlarded with petit mal and/or petit mal equivalent, and psychomotor seizures. Surgery has not proved helpful for petit mal or petit mal equivalents alone or for pyknolepsy and certain of the so-called epileptic equivalents, e.g. narcolepsy and cataplexy.

Pathology

The "firing point" *may* be macroscopically or microscopically visible in the form of meningeocortical adhesions, a cortical or subcortical cicatrix, gliosis, a cystic degenerated or atrophic site, blood vessel malformation, dysplasia in the nature of hamartoma, and so on; or it *may not* be demonstrable grossly or by currently available histopathologic studies. In the latter case it may be nonetheless pathological, revealed as such by electrical stimulation or modern biochemical and biophysical techniques.

Although the firing point is recognizable as an integral, pathogenetic component of a seizure, it manifestly cannot produce a seizure by itself. Contributing factors (e.g. physiologic "tides," such as hypoglycemia) and a number of inadvertent factors (e.g. caffein and other stimulants of analeptic type) appear to be essential to "priming the pump."

Surgical Measures

A surgical attack is warranted only when the epileptogenic focus can be topically localized. Ideally, several independent preoperative inquiries should provide mutually confirmatory data about the locus of the firing point. The inquiries conventionally used include (*a*) a dependable, preferably confirmed, description by the patient or associates of a consistent pattern of onset of "spontaneous" seizures with "focal" (sensory or motor) features; (*b*) observation by the physician of the pattern of onset of seizure (whether "spontaneous" or induced by hyperventilation, hyperhydration or Metrazol potentiation); (*c*) neurologic signs, such as postictal paralysis; (*d*) focal, abnormal shadows on the ordinary x-ray films of the skull, suggestive of intracranial calcification, foreign bodies, defects of the bony vault, and so on; (*e*) excessive circumscribed pooling of subarachnoidocortical gas (air) or other abnormalities (e.g. cysts and distortions of the ventricular system) as revealed by pneumoencephalography or ventriculography; (*f*) electrographic dysrhythmia, especially that characterized by repetitive "spikes" or "spikey" electrical discharges and revealed by standard scalp, cortical, subcortical or "deep" leads (basal ganglionic, thalamic and pretectal); and (*g*) cerebral angiography, showing deformation, distortion or other anomaly of the vessels of the brain at a site consistent with that of, or suggested by, other techniques of inquiry.

If the foregoing procedures permit a reasonably sound inference as to the site of "the epileptogenic focus," operation may be contemplated, provided it is not located within the brain area essential to the preservation of symbolic speech.

At operation an area of cortex is exposed, generously encompassing the suspected "epileptogenic focus." Inspection, palpation, electrocorticography and deep pick-up electrode studies are now directed at identifying the firing point. Bipolar cortical stimulation is also used with a view to detecting a hypersensitive zone which, upon being stimulated, results in a clinical seizure or seizure-fragment that closely simulates the patient's "spontaneous" convulsions.

It is desirable to perform the operation without benefit of general anesthesia. The cooperation necessary for such can rarely be obtained in children under the age of 10 years and appreciably less often than wished for in older children (up to the age of 13 years). When indicated, general anesthesia avoiding barbiturates may be used, despite the handicaps imposed thereby. Many older children cooperate well during local anesthesia.

The most successful cases are those in which a macroscopic epileptogenic focus is apparent and excisable. The surgeon aims to remove all *abnormal and sufficient borderline tissue* to get beyond the regions that

exhibit electrographic spikes and other dysrhythmias considered significant of "electrical seizures." The resection may be relatively small; on the other hand, it may be of gyral, lobular, lobar and subtotal hemispheral dimensions. Induction of hemiparesis or hemihypesthesia may be justified when relief of intractable seizures appears to be a paramount issue at stake.

Benefits in the abolition or alleviation of seizures may be expected in 45 to 70 per cent of cases selected as outlined above. An operative mortality rate of slightly less than 5 per cent should be contemplated. The remainder of cases receive either no benefit or but slight to moderate reduction in the frequency, severity and types of seizure.

Postoperatively, anticonvulsant medication should be administered for 9 to 12 months, after which it may be gradually withdrawn. If seizures recur, it must be resumed. In this case, operation cannot be counted as optimally successful. Reoperation with wider surgical excision may then be in order.

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DIAGNOSIS AND MANAGEMENT OF CONVULSIVE DISORDERS

With Special Emphasis on Seizures Amenable to Specific Therapies

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Seizures are one of the more common symptoms encountered in children with disease or functional disturbance of the central nervous system. More than 90 per cent of convulsive disorders have their onset during the early years of life, and one out of every 15 children admitted to hospital has a history of seizures.[27]

The basic mechanism common to all seizures is an alteration of neuronal activity originating from disturbances of physicochemical function within the brain. The nature of this abnormality is not clearly understood. In a high percentage of patients a predisposition to seizures appears to be inherited, and the importance of a constitutional factor in etiology is well established.[24] In many patients additional factors may be contributory, and, in some, acquired abnormalities alone may be sufficient to induce a seizure.

For the purpose of diagnosis, convulsive disorders are often classified as symptomatic or cryptogenic, according to the presence or absence of organic factors which may be of importance in the occurrence of the attacks. From the point of view of management and prognosis, patients with seizures of the symptomatic type should be subdivided further: (*a*) those with biochemical, physiologic or anatomic disorders which

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may be amenable to specific therapies; and (*b*) patients with local or diffuse cerebral abnormalities which are not amenable to removal or specific correction and in whom treatment is largely empirical.

A list of diseases and conditions which may be accompanied by seizures is extensive; Tables 10 and 11 show the commonest of these disorders. Disease processes which result in a temporary and reversible injury to the brain are associated with seizures only during the acute episode, whereas cerebral disorders which are chronic in type may predispose to recurrent seizures. Arrival at an accurate diagnosis depends upon a thorough study of the patient and correct interpretation of evidence obtained from the personal and family history, the examination, and certain laboratory procedures.

TABLE 10. *Etiologic Classification of Seizures Amenable to Specific Therapies**

Fever and extracranial infection	Tonsillitis, otitis media, pneumonia
Intracranial infection	Meningitis
Electrolyte imbalance	Water intoxication, hyponatremic and hypernatremic states
Metabolic disorder	Hypocalcemia, hypoglycemia, pyridoxine dependency, phenylpyruvic oligophrenia
Toxic encephalopathy	Lead, thallium
Hypertensive encephalopathy	Acute glomerulonephritis
Acute anoxia	Anesthesia, congenital heart disease
Light stimulus	Bright sunlight
Intracranial structural lesion	Hematoma, abscess, neoplasm, vascular malformation, cyst
Miscellaneous	Emotional disturbance, allergy

* Empirical anticonvulsant therapy often required in addition.

TABLE 11. *Etiologic Classification of Seizures Amenable to Empiric Therapies*

Undetermined origin:	
Cryptogenic (idiopathic)	
Known contributory brain lesions:	
Post-traumatic	Laceration
Posthemorrhagic	Injury, hemorrhagic disease, ruptured aneurysm
Postanoxic	Asphyxia neonatorum
Postischemic	Thrombosis, embolism, vasospasm
Postinfective	Meningitis, encephalitis, encephalopathy, immunizations, abscess, congenital syphilis
Post-toxic	Bilirubin, lead, thallium
Congenital	Aplasia, porencephaly, hydrocephalus, Sturge-Weber vascular anomaly, tuberous sclerosis
Degenerative	Lipidoses, leukoencephalopathies
Parasitic	Toxoplasmosis, cysticercosis
Neoplastic	Tumors not amenable to surgery

DIAGNOSIS

The diagnostic procedures are somewhat dependent upon the age at onset, the type and the frequency of the seizures. The following examinations are included in a complete study: (1) history, and physical and neurologic examinations (see also p. 471); (2) urinalysis, determinations of blood glucose and calcium, and serologic test for syphilis, x-rays of skull, cerebrospinal fluid examination; (3) electroencephalogram, with activating procedures such as hyperventilation, sleep and photic stimulation; (4) pneumoencephalogram, ventriculogram or cerebral angiogram.

Electroencephalography or angiography should be performed in the following circumstances and when the necessity for surgical therapy is considered probable: (*a*) if abnormal neurologic signs are progressive and indicative of a focal lesion; (*b*) if a focal area of cerebral calcification or bony rarefaction is apparent in the skull x-ray and is indicative of a lesion amenable to surgical therapy; (*c*) if the pressure or protein content of the cerebrospinal fluid is increased and cannot be explained by a diffuse infective process or encephalopathy.

Focal seizures alone are not sufficient indication for neurosurgical diagnostic procedures. The patient must be observed for development of more reliable criteria of an expanding lesion, and repeated neurologic examination over a period of several months may be needed before a definite diagnosis is established in some cases.

Age at Onset. The age at the time of onset of seizures has some significance in the differential etiologic diagnosis and the nature of the clinical manifestations. In the newborn period certain enzyme systems in the brain which may be intimately concerned in the basic mechanism of seizures are incompletely developed.[37] In the immature infant the tendency to seizures is minimal and the major tonic-clonic seizure is uncommon; convulsive activity is manifested by minor patterns such as tremor, hyperkinesia and myoclonic jerks. From birth to six months of age seizures are frequently associated with structural or metabolic disorders of the brain, and inability to recognize some contributory etiologic factor is rare. Children between six months and three years of age are susceptible to febrile seizures; and bacterial meningitis is a relatively frequent cause at this age. In older children the tendency to seizures is maximal, associated anatomic or biochemical defects are diagnosed less frequently, and seizures of undetermined origin are more common.

SEIZURES AMENABLE TO SPECIFIC THERAPIES

Many factors are known which tend to lower the threshold to seizures, and some are susceptible to correction or removal. In the treat-

ment of seizures associated with functional or structural abnormalities of the brain, anticonvulsant drugs are sometimes ineffective when administered alone, but are of value as an adjunct to specific therapies.

The commonest convulsive disorder in childhood of the type amenable to specific therapy is the febrile seizure.

FEBRILE SEIZURES

The significance of seizures associated with fever in infants and young children is controversial.[26] Although some investigators attest to the benign nature and sanguine prognosis of febrile seizures,[14, 27] others emphasize the gravity of such symptoms and regard them as evidence of an organic cerebral lesion.[43] The diversity of opinions may be explained principally by the different criteria used in selection of cases and by differences in definition of terms.[35]

The relation of febrile convulsions to other epilepsies is widely disputed. Some authors regard them as a specific disorder distinct from the epilepsies, whereas others have used the terms "mild" or a "pure" form of epilepsy.[16, 26] In studies by Livingston[27] seizures which are prolonged, focal or associated with electroencephalographic abnormalities are not accepted as febrile in type. They are considered "epileptic seizures" in which fever acts as a precipitating factor. The diagnosis of "simple febrile convulsions" is restricted to patients under six years of age with short, generalized seizures and a normal electroencephalogram. Similarly, Prichard and McGreal[44] divide febrile convulsions into two categories, simple and atypical, and Friderichsen and Melchior[14] omit from their series children with evidence of birth trauma and those with cryptogenic epilepsies.

Classification of febrile convulsions into subgroups on the basis of the severity of the seizure, electroencephalographic abnormalities and other criteria is of practical value in the assessment of prognosis. In our understanding of the mechanism of febrile seizures, however, this arbitrary division of cases is confusing, and data derived from the study of an unselected series of patients are more revealing.[35]

Etiology and Mechanism. The height of the body temperature is the essential factor contributing to the etiology of febrile seizures.[32] Children with a low threshold may convulse with minimal degrees of fever, whereas those with a high threshold have seizures when the body temperature exceeds 105° F. or more.

Additional factors which may be important in the etiology are infection, allergy and electrolyte imbalance.[33] The role of infection is probably nonspecific and is related to the concomitant occurrence of fever. In 70 per cent of patients the febrile seizure occurs with acute infection of the upper respiratory tract. The frequency of association with

acute tonsillitis, pharyngitis and otitis media may be explained by the prevalence of these infections in young children.

That hypersensitivity reactions may be important in the initiation of seizures in some patients is suggested by the relatively high incidence of allergic symptoms in our series of patients and in their relatives. Immune reactions may occur to the toxic products of infective organisms, and the patient may be allergic to penicillin, aspirin and other agents used in the treatment of the febrile illness. The alteration in the permeability of cell membranes associated with allergic reactions and infection[20] may result in a disturbance of the balance of water and electrolytes in the brain. Low levels of serum sodium observed in close relation to the occurrence of febrile seizures emphasize the hazards of electrolyte imbalance and water intoxication.[8, 33] In children susceptible to febrile seizures rapid administration of hypotonic parenteral solutions during acute febrile episodes should be avoided.

Threshold to Febrile Seizures. Age, and immaturity of the balance of electrolytes in the brain, sex, heredity and acquired brain lesions are important determinants of the threshold to febrile seizures. Infants and children between six months and five years are commonly affected, and a recurrence above nine years is rare. Males are affected twice as frequently as females.

In contrast to a number of previous reports,[26, 27] a family history of febrile seizures, obtained in one third of our patients, was equally prevalent in those who suffered from nonfebrile as well as febrile seizures. Further, a history of nonfebrile seizures in the family was elicited no less frequently than that of febrile seizures. It is suggested, therefore, that the genetically determined abnormality which may result in a low threshold to febrile seizures is of the same nature as that which may underlie susceptibility to spontaneous seizures in some patients. A distinction between febrile seizures and the epilepsies based on this genetic evidence is unjustified. In febrile states the metabolic processes concerned in the mechanism of seizures are accelerated, and the tendency to seizures is augmented and may be manifested at an earlier age.

Acquired injury to the brain was contributory in 20 per cent of patients. In children who subsequently had nonfebrile seizures the incidence of cerebral birth trauma was twice that found in the group with febrile seizures alone, but the difference was not significant. It seems, therefore, that the threshold to febrile seizures may be lowered by cerebral defects which are inherited or acquired and functional or structural.

Prognosis. Febrile seizures are likely to recur in 50 to 60 per cent of patients, but only 10 to 20 per cent will have more than 4 seizures. During a single febrile illness the chance of seizure recurrence is about 1 in 3.

Apart from the rare postictal paralysis, the most serious complication

is the occurrence of seizures without fever. In an unselected group of patients nonfebrile seizures may be expected to occur in 20 per cent, and these may recur frequently in 5 per cent. In addition to convulsive seizures, recurrent attacks of abdominal pain and vomiting and episodic disturbances of behavior occur in 20 and 35 per cent of patients, respectively, and are suggestive of a concomitant autonomic or diencephalic seizure disorder.

Epileptiform discharges in the electroencephalogram are much more frequent in patients with spontaneous seizures than in those with febrile seizures alone. Abnormalities in the electroencephalogram and febrile seizures of long duration are the principal criteria indicative of a poor prognosis. The frequency of febrile seizures may be important, but the occurrence of a focal seizure pattern is unrelated to the subsequent development of nonfebrile seizures.

The harmfulness of convulsions associated with fever is emphasized in some reports,[13, 45] and the occurrence of nonfebrile seizures has been attributed to brain injury sustained during an initial febrile convulsion.[23] That hyperpyrexia with prolonged convulsions may result in neuronal necrosis and permanent brain damage is well known. Present evidence suggests, however, that febrile seizures generally do not predispose to spontaneous seizures, but that this complication is dependent upon genetic or acquired etiologic factors common to both types of seizures.

Treatment. Prevention of a rise in body temperature above the threshold level at which seizures have previously occurred is the principal aim in prophylactic therapy. Specific forms of treatment include the following: antipyretics to inhibit heat production in the presence of infection, anticonvulsants to raise the threshold convulsive temperature, and antibiotics to combat infection.

Aspirin, phenobarbital and Dilantin, the therapeutic agents most commonly used, have been found inadequate.[36] The prophylactic value of phenobarbital or Dilantin administered continuously in repeated daily doses was not superior to that of phenobarbital given intermittently at the time of febrile episodes. Seizure control was poor and of questionable degree in patients treated by either method.

Continuous administration of anticonvulsant drugs for the prophylaxis of fever-induced seizures appears unwarranted. Such therapy should be reserved for patients with a particularly low threshold whose seizures occur with a small rise in temperature of questionable significance, and for patients who have suffered a nonfebrile seizure in addition. In patients with a previous history of febrile seizures uncomplicated by spontaneous seizures, anticonvulsant drugs should be administered in relatively large doses at the earliest signs of infection and until the fever has defervesced. Pyrictal (BW No. 401), which is a new drug[34] with

specific activity against fever-induced seizures in animals, has both antipyretic and anticonvulsant properties in dosages which are nonsedative. On the basis of laboratory tests and preliminary clinical trials, Pyrictal appears superior to agents commonly used for the prevention of febrile seizures. The initial dose advised is 15 to 20 mg. per kilogram orally, and smaller doses are repeated at intervals while infection persists.

The action of antifebrile-anticonvulsant drugs should be augmented by baths of tepid water and other simple measures for the facilitation of loss of body heat. Antibiotics may be essential for the treatment of an associated bacterial infection. Since penicillin may possibly increase the tendency to seizures in some circumstances,[51, 26, 34] the avoidance of unnecessarily large doses in young infants is probably advisable.

INTRACRANIAL INFECTIONS

Convulsions are a common complication of bacterial meningitis (see also p. 605) in children. When they are prolonged, recurrent, and resistant to therapy, the prognosis is invariably grave. Large and depressant doses of barbiturates are usually required for the control of such seizures, and the necessity for preventive therapy is emphasized. Antibacterial therapy should be complemented by the antifebrile-anticonvulsant treatment outlined for febrile seizures. Administration of barbiturates in divided daily doses from the onset of the disease has been shown to reduce the incidence of mortality and of postmeningitic sequelae significantly.[40]

Subdural effusion which may accompany or follow the acute phase of the illness is sometimes associated with convulsions. The diagnosis is suspected when fever, irritability, drowsiness and vomiting are persistent, and when convulsions and hemiparesis are associated with an increase in the circumference of the head. A subdural tap will confirm the diagnosis. The management is essentially the same as in subdural hematoma of infancy, except that many patients recover on repeated tapping and do not require major surgical intervention (see also p. 551).

Hyponatremia is a complication of meningitis in children,[39] and the concomitant disturbance of electrolyte balance tends to lower the threshold to seizures.[33] It may be avoided by early determination of electrolyte levels and administration of calculated amounts of parenteral fluids.

ELECTROLYTE IMBALANCE

Maintenance of the balance of water and electrolytes is important in the proper management of seizures of all types.[8, 30, 33] The threshold to

seizures is primarily dependent upon the relative concentrations of sodium within the nerve cell and in the extracellular fluid of the brain. In animals with experimental seizures a low threshold is related to a low level of serum sodium and a fall in the ratio of extracellular to intracellular sodium in the brain.[55]

Hyponatremia and Seizures

Hyponatremia and consequent alteration in the balance of electrolytes at a cellular level may be associated with convulsions in the following conditions: (1) loss of sodium as a result of diarrhea or prolonged fever and excessive sweating, or as a complication of central nervous system disease, such as encephalitis and bulbar poliomyelitis, (2) reduced intake of sodium due to inadequate diet or improper fluid and electrolyte therapy, (3) overhydration due to excessive thirst or tap water enemas and improper fluid therapy, (4) a redistribution of intracellular and extracellular fluids and an expansion of the plasma volume due to fever and acute infections which do not involve the nervous system directly, and (5) retention of water and acute expansion of the extracellular fluid volume associated with acute infections of the central nervous system, and the administration of morphine and ether during operation.[8, 19, 30, 39, 50]

Symptomatic hyponatremia has been reported in children with acute bacterial meningitis due to Haemophilus influenzae type B and pneumococci and with measles encephalitis.[39] Loss of sodium from the body was not remarkable, and the hyponatremia was thought to represent a primary water retention due to stimulation of the supraoptic nuclei of the hypothalamus and excessive release of antidiuretic hormone. A similar mechanism may underlie the complication of water intoxication in infants and children undergoing operation;[19] excessive antidiuretic activity may be stimulated by ether anesthesia or preoperative or postoperative administration of morphine.

The manifestations of water intoxication include drowsiness, confusion, irritability, stupor, convulsions, papilledema, and elevation of the cerebrospinal fluid and blood pressures. The convulsions are resistant to anticonvulsant drugs, and correction of the electrolyte imbalance is essential for their control.

In conditions known to predispose to hyponatremia and convulsions rapid administration of hypotonic fluids by oral or parenteral routes should be avoided. If hyponatremia has developed, the electrolyte balance is corrected slowly, using a 3 per cent solution of sodium chloride with added potassium. Phenobarbital, used as an adjunct to fluid therapy, may stabilize the nerve cell membrane and facilitate correction of the balance of intracellular and extracellular electrolytes.

Hypernatremia and Seizures

The cause of seizures in association with hypernatremic states is variable and sometimes not clearly defined. Hypernatremia has been observed with primary disease of the central nervous system and particularly with involvement of the frontal lobes and the hypothalamus;[7] seizures may occur as a manifestation of the underlying cerebral pathology. Alternatively, hypernatremia with associated symptoms of central nervous system dysfunction may result from dehydration and sodium retention secondary to diarrhea,[48] reduced water or excessive salt intake,[12] the feeding of a high-solute skimmed-milk formula,[6] and impaired renal function. A subdural hygroma as a complication of hypertonic dehydration appeared to explain the occurrence of seizures in some infants.[12]

The *diagnosis* of hypertonic dehydration in infants with diarrhea is made on the basis of the abnormal neurologic signs and the absence of signs of intracellular fluid loss and obvious dehydration. Lethargy, irritability, coma, depressed tendon reflexes, and muscular rigidity are frequent abnormal findings. The skin is dry, but has normal elasticity. The eyes are not sunken, and the tension of the fontanel is usually normal. A serum sodium concentration of 150 mEq. per liter or higher confirms the diagnosis. Restoration of normal concentrations is difficult and hazardous. It is frequently complicated by convulsions, despite levels of serum sodium which are higher than normal.[6, 53] The seizures may be explained by cerebral cortical damage and an alteration in permeability of the nerve cell membrane. The relative concentrations of intracellular and extracellular sodium, of fundamental importance to neuronal excitability, may thus be disturbed, and the paradoxical occurrence of seizures with high levels of serum sodium may be reconciled.

Treatment is similar to that used in acute renal failure, but the balance of electrolytes must be corrected slowly. Water is provided for the replacement of that lost, plus a small daily increment of 10 to 20 ml. per kilogram to initiate the repair of water depletion. Sodium administration is limited and potassium administration deferred until return of good renal function.[48] Treatment with anticonvulsant drugs during correction of the fluid and electrolyte balance may be of value for the prevention of seizures, and calcium gluconate may be required for the treatment of a concomitant hypocalcemia.[12] In some cases seizures have been controlled by administration of a 3 per cent solution of sodium chloride and by temporary elevation of the concentration of serum sodium.

METABOLIC DISORDERS

Hypocalcemia

Calcium is necessary for the selective permeability of cell membranes to sodium and potassium and the preservation of the normal function-

ing of the nervous system. A fall in the concentration of calcium in the serum causes an instability of cell membranes and signs of neuromuscular irritability.

Convulsions associated with a reduction of the diffusible, ionized form of calcium may occur in the following conditions: (1) neonatal tetany, (2) cryptogenic or traumatic hypoparathyroidism, (3) pseudohypoparathyroidism, (4) rickets, (5) steatorrhea, (6) during treatment of acidosis with dehydration, (7) during treatment of hypertonic dehydration, and (8) chronic renal insufficiency. The convulsions are usually clonic and generalized, but may be focal in pattern. Apart from the newborn period, hypocalcemia is a relatively uncommon cause of seizures in childhood. The diagnosis should be suspected and the serum calcium estimated, however, when seizures are resistant to anticonvulsant drugs and are accompanied by additional signs of tetany and related disease states.

Hypoglycemia

The criteria for the diagnosis of hypoglycemic convulsions include the following: (1) a significant reduction in the blood sugar level with each convulsion, (2) induction of a seizure by fasting, and (3) rapid control of the seizure by administration of glucose. Hypoglycemia may be caused by hyperinsulinism, hypopituitarism, adrenocortical insufficiency and glycogen storage disease.

Pyridoxine (Vitamin B_6) Deficiency or Dependency

Convulsions in young infants due to pyridoxine deficiency were common between 1950 and 1954. They occurred only in infants fed a liquid milk in which the pyridoxine had been destroyed during the process of manufacture. Since the withdrawal of this preparation, no further case has been observed.

Convulsions occasionally occur in infants as the result of a pyridoxine-dependent state;[1] the requirement of pyridoxine exceeds the usual need. The infant is irritable, has hyperactive tendon reflexes, and may be retarded in development. The diagnosis is confirmed by the tryptophan-loading test and an immediate beneficial response to administration of vitamin B_6. Urinary excretion of xanthurenic acid, an abnormal product of the metabolism of tryptophan, is increased in states of vitamin B_6 deficiency, and the excretion is accentuated after administration of dl-tryptophan. In infants with vitamin B_6 dependency a supplement of 1 to 1.4 mg. daily is required to prevent the excretion of xanthurenic acid, whereas normal infants receiving 0.2 to 0.5 mg. of vitamin B_6 daily fail to excrete the acid.

At least two to three times the minimum requirement of vitamin B_6

should be provided in the diet to prevent convulsions, and this is contained in the usual evaporated milk mixtures. Since occasional instances of excessive requirements are known to occur, a therapeutic trial of 5 to 10 mg. daily of pyridoxine hydrochloride is advised in all infants with convulsions of undetermined cause.

TOXIC FACTORS

Seizures are prominent manifestations of poisoning with lead, thallium, DDT and other insecticides, and may occur also with salicylate intoxication and during therapy with steroids and tranquilizing drugs.

Lead Poisoning

Acute encephalopathy due to lead is not uncommon as a cause of seizures in children, and a high level of suspicion is important in diagnosis. It is worthy of emphasis that no one sign of lead poisoning is pathognomonic; all can be simulated by other diseases. The possiblity of cerebral tumor or hypertensive encephalopathy must be considered in a child with papilledema and convulsions despite concentrations of lead in the blood and urine which are higher than normal.

The convulsions may be generalized or focal in pattern and are difficult to control. Additional signs include papilledema, bulging of the fontanel, cervical rigidity, hemiparesis, tremors and ataxia, and the blood pressure is often raised. The urine contains protein and sugar. The cerebrospinal fluid is under increased pressure, and the protein is greatly increased. The cell count is variable and may be normal or only slightly elevated; 100 or more lymphocytes are occasionally found.

The immediate response to *treatment* with anticonvulsant drugs and edathamil (Versenate) is generally unsatisfactory, and the mortality rate in acute encephalopathy with convulsions is high. The permeability of the blood-brain barrier to edathamil is low, and amelioration of symptoms and signs is often delayed. Early surgical intervention and the use of bilateral decompressive craniectomy have resulted in a significant reduction in mortality in some series of cases.[29] The recognition of pica as a common prelude to plumbism, early diagnosis,[4, 54] and removal of the source of lead before the advent of encephalopathy may be the only certain methods of prevention of permanent neurologic sequelae.

Thallium Poisoning

Convulsions may be associated with other signs of central nervous system disturbance and with alopecia in approximately one third of patients with thallotoxicosis. The source of the poison is usually a ro-

denticide containing thallium and prepared in the form of a vanilla-flavored wafer, syrup or paste.

Diagnosis is established by extraction of thallium from the urine and its subsequent estimation in a flame spectrophotometer. The following *treatment* has been recommended: (1) gastric lavage, (2) potassium chloride, 3 to 5 gm. daily, and (3) Dithizon, 10 mg. per kilogram twice daily, for at least 5 days.[5] Anticonvulsant drugs should also be administered.

Phenothiazine Poisoning

The phenothiazine derivatives used as tranquilizing agents include chlorpromazine (Thorazine), prochloperazine (Compazine), promazine (Sparine) and perphenazine (Trilafon). Seizures have been reported in children receiving these drugs for the treatment of nausea, vomiting, anxiety and restlessness.[47] Tremor, athetosis, dystonia, rigidity and trismus are more common manifestations of toxicity.

The *diagnosis* may be facilitated by addition of a 10 per cent solution of ferric chloride to the urine;[38] a red-purple color develops when the phenothiazine derivatives are excreted. Ketone bodies which have a similar color reaction with ferric chloride may be removed by boiling the urine; salicylates impart a blue-purple color. Recovery is rapid after withdrawal of the drug. Phenobarbital may be required for the treatment of persistent convulsions, and Cogentin may be used for the control of extrapyramidal symptoms.

"HYPERTENSIVE" ENCEPHALOPATHY

Acute glomerulonephritis may be complicated by convulsions which are usually clonic and generalized in pattern, sometimes focal, and often refractory to conventional anticonvulsant drugs. At the onset of the convulsions a significant degree of hypertension may not be demonstrable, and the exact mechanism of "hypertensive" encephalopathy in acute nephritis is not clearly understood. Treatment with Apresoline, or magnesium sulfate by intramuscular injection, is indicated whenever the diastolic blood pressure is 95 mm. of mercury or the systolic pressure is 140 or higher. Depression of the deep tendon reflexes is an early sign of overdosage of magnesium sulfate. Phenobarbital may prove beneficial as an adjunct to more specific therapies.

TONIC DECEREBRATE AND OPISTHOTONIC SEIZURES

Decerebrate postural seizures are attacks, usually of brief duration, in which the arms are extended at the patient's side and the hands are

pronated, the legs are extended, and the feet held rigidly in plantar flexion. They are of serious prognostic import, and are due to acute compression or ischemia of the mibrain. An expanding lesion such as cerebral edema or tumor may be responsible, and may require surgical or other specific therapy.

In opisthotonic postural seizures the neck and spine are arched backward and there is no pronation of hands or plantar flexion of feet. This seizure pattern may be a sign of irritation of the brain stem as the result of meningitis or subarachnoid hemorrhage. Specific forms of therapy may be required.

PHOTOGENIC SEIZURES

Seizures in response to photic stimulation may occur spontaneously in some patients sensitive to ordinary light intensities, and may be induced in other patients only with illumination of high intensity.[2] In periods between seizures the *diagnosis* may be confirmed by the appearance of epileptiform discharges in the electroencephalogram in response to photic stimulation with white or colored lights. The relative sensitivity to various parts of the spectrum is determined, and glasses, selected to filter out the color responsible, are worn whenever the patient is exposed to bright light. The *treatment* is specific and successful, whereas empiric therapy with anticonvulsant drugs is of little value.

SEIZURES AMENABLE ONLY TO EMPIRIC THERAPIES

In patients with seizures of undetermined origin and in those with etiologic factors for which there is no specific therapy, treatment with drugs is largely empirical. The choice of anticonvulsant medication is dependent upon the clinical pattern of the seizure, and an accurate description of the attack by a reliable observer is of utmost value in the management of drug therapy.

SEIZURE PATTERNS

The clinical manifestations of convulsive disorders are diverse, but in most patients the seizures can be classified in one of five groups as follows: major, minor, autonomic, psychomotor and focal seizures.

Major Seizure Patterns

GENERALIZED CONVULSIONS. Grand mal seizures constitute the largest proportion of attacks. A sudden loss of consciousness is followed by tonic and/or clonic spasms of the musculature with or without tongue

biting, urinary or fecal incontinence and excessive salivation. On regaining consciousness the child may be dazed, confused and drowsy, and may lapse into a heavy sleep, to awaken several hours later. Electroencephalographic seizure discharges[22] may consist of high voltage spikes, spike and wave, slow wave or sharp wave patterns. Phenobarbital, Dilantin and Mysoline are the most effective drugs in treatment.[18, 42]

Status Epilepticus. This is a state of recurring generalized convulsions between which the patient does not completely regain consciousness. When the pattern of the seizures is principally tonic and is associated with frequent episodes of apnea, status epilepticus is a dangerous complication and should always be treated as an emergency. It may be precipitated by too rapid withdrawal of phenobarbital, Dilantin or Mysoline, but sometimes develops without an apparent cause. Patients with organic brain lesions are most susceptible.

Anticonvulsant medication is administered early in optimum doses by the parenteral route. A relatively large single dose is far superior to small divided doses given at intervals. The choice of drug depends largely on the experience of the physician. We have obtained most success with the use of phenobarbital sodium; ½ to 1 grain per year of age up to a maximum of 4 grains is an approximation of the dose usually required. The subcutaneous route of administration is used when the seizure is moderately severe and mainly clonic in pattern. Intravenous injection of anticonvulsant drugs is sometimes attended by apnea, and this route is advised only in the treatment of severe, protracted and mainly tonic seizures; the drug is administered slowly. When necessary, half the initial dose may be given after an interval of 20 or 30 minutes, and the patient is observed carefully for signs of respiratory depression. Alternative drugs include Sodium Amytal, paraldehyde and parenteral Dilantin. Ether anesthesia may be essential for the control of status epilepticus in some cases. Factors such as fever, electrolyte imbalance and hypoglycemia, which may predispose to status epilepticus should be treated specifically.

Infantile Spasms. Lightning major seizures, massive myoclonic jerks and massive spasms are some of the alternative terms used for this seizure pattern, which is characterized by a sudden, transient, bilaterally symmetrical and usually repetitive contraction of most of the body musculature. Flexion of the head and trunk with adduction and flexion of the limbs is the most frequent manifestation, but abduction or extensor movements, tremors and opisthotonic spasms are also seen. The attacks occur mainly during the first 2 years of life, and 85 per cent begin in the first year. Generalized, focal and other seizure patterns may precede, accompany or follow the infantile spasms. Mental deterioration is a frequent concomitant. An electroencephalographic pattern termed hypsarrhythmia is a characteristic finding of grave prognostic import.[3, 15]

The record is diffusely abnormal with bursts of high voltage slow activity, spikes occurring independently in all leads, and periods of relative electroencephalographic silence. The etiology is unknown, and the evidence for cerebral injury at birth or during prenatal development reported in approximately 50 per cent of patients is only presumptive. Neuropathologic structural changes were minimal in one case, and some undetermined disorder of cerebral metabolism seemed the most likely explanation for the seizures.

The response to *treatment* is generally poor. Combinations of Gemonil and Mebaral[42] and of Dilantin and Diamox have sometimes proved successful. Pyrictal with Dilantin may also afford relief. A beneficial response to steroid therapy has been reported.[28] Spontaneous remission of infantile spasms occurs at two or three years of age, but the continuation of anticonvulsant therapy for major generalized seizures is often required.

Minor Seizure Patterns

Petit mal attacks occur principally in children of 4 to 12 years of age and rank second to grand mal in order of frequency.

Petit Mal.. This term originally was used to describe all minor seizures, but now is reserved for the brief lapse of consciousness or "absence" associated with the 3-per-second spike-and-wave pattern in the electroencephalogram. The lapse of consciousness occurs without warning, and may be accompanied by slight rhythmic movements of the eyelids, eyebrows, lower jaw and upper limbs. Voluntary purposive movements are interrupted, but posture is not disturbed. Occasionally a history of birth injury or encephalitis may be obtained, but generally a genetically determined predisposition to seizures is the only finding.

A favorable therapeutic response to Tridione and Paradione is the rule, but the efficacy of these drugs is limited by their toxicity. The hazard of the remedy must be compared with the severity of the symptoms, and in patients with infrequent seizures of the petit mal type the use of a potentially toxic therapeutic agent cannot be condoned. Less toxic agents such as Miltown,[41] Prenderol[42] and Milontin are often advised as initial therapies, and Paradione or Tridione is used in patients with frequent seizures resistant to other drugs.

Spontaneous improvement may be expected in adolescence or early adulthood, but a tendency to grand mal seizures may develop. The management of patients with both petit mal and grand mal is often troublesome. Dilantin exacerbates petit mal, and Tridione may augment the tendency to grand mal. Phenobarbital, Mebaral or Mysoline may be beneficial, but a combination of drugs such as phenobarbital and Tridione is more successful. The appearance of multiple-spike com-

plexes in the electroencephalogram of a child with petit mal may herald the occurrence of major convulsions and indicates the need for prophylactic therapy with phenobarbital in addition to Tridione.

Petit mal status consists of an almost continuous series of petit mal discharges which may persist for as long as three or four days. An intravenous preparation of Tridione or parenteral phenobarbital is usually required for control of the attack.

Akinetic Seizures. These attacks are characterized by a transient loss of postural tone with a sudden fall to the floor or a nodding of the head. The episodes are brief, and consciousness and posture are regained almost instantaneously. Major grand mal, focal seizures and minor seizures of other types are often associated, and mental retardation and motor impairment indicative of brain injury are not unusual. The electroencephalographic pattern most frequently seen is the 2-per-second, slow spike-and-wave, but focal spikes and other discharges also occur. The response to treatment with anticonvulsant drugs is poor. Mysoline, Dilantin and Diamox are more effective than Tridione.

Myoclonic Seizures. Myoclonus is a sudden involuntary contraction of the muscles of the limbs, trunk, neck or face without apparent loss of consciousness. It may be the only manifestation of a seizure disorder, but is often associated with major seizures and may increase in severity and frequency just before the onset of a grand mal attack.

The *etiology* is often undetermined and unrelated to structural abnormalities of the brain. In some cases, however, the underlying pathology is a primary degeneration of nerve cells, which may be familial. The development of symmetrical myoclonus in association with progressive dementia, pseudobulbar paralysis and quadriplegic rigidity in flexion is characteristic of juvenile amaurotic familial idiocy, subacute inclusion-body encephalitis, and the myoclonus epilepsy of Unverricht.[52]

The electroencephalogram may be of value in *differential diagnosis*. A diffusely abnormal record with slow waves, triphasic complexes, and intervals of electrical silence is indicative of a progressive degenerative disease, whereas synchronous discharges of slow waves and multiple spikes are commonly associated with cerebral pathology which is nonprogressive and sometimes cryptogenic.

Treatment with phenobarbital or Mysoline should be complemented with Gemonil or Pyrictal, but the response to medication is usually poor.

Abortive Major Seizures. A lapse of consciousness associated with minimal convulsive movements and little evidence of postictal sequelae may represent an abortive grand mal seizure. The differentiation from petit mal is important in management and is made on the basis of the electroencephalogram or the response to a therapeutic trial of Dilantin.

BREATH-HOLDING SPELLS. In children between three months and five years of age, crying spells may end suddenly with a period of apnea and may be associated with transient unconsciousness with flaccidity or convulsions. A precipitating factor which arouses an acute emotional response may be present, but is not invariable. Apnea may follow prolonged crying, but sometimes occurs after a single expiratory gasp. Transient unconsciousness with flaccidity or convulsive movements appears to be unrelated to the duration of apnea and the degree of cyanosis.

The nature of these episodes is not clearly understood. In many instances the convulsions cannot be explained satisfactorily on the basis of anoxia. A psychogenic factor may be contributory in older children, but the absence of an antecedent emotional disturbance and an onset in early infancy in some patients militate against this proposed mechanism. The normal appearance of the electroencephalogram in the majority of patients does not necessarily exclude a seizure discharge originating in the respiratory centers of the medulla and an epileptogenic basis for the attacks.

Treatment is dependent upon the severity and frequency of attacks. Phenobarbital should be administered during the acute episode if a convulsive seizure occurs and is more than transient in duration. A trial of continuous anticonvulsant therapy is advised[10] in patients with spells of apnea which occur at frequent intervals and particularly when convulsive movements are associated. The *prognosis* is good, and subsequent development of spontaneous convulsions is rare.[27] Episodic disturbances of behavior are not infrequent, however, and may possibly represent a seizure disorder.

Autonomic Seizures and Seizure Equivalents

Paroxysmal recurrent attacks of abdominal pain and cyclic or periodic vomiting may be manifestations of an autonomic seizure disorder.[31, 49] The diagnosis is dependent upon the following criteria: (1) the episodic nature of the attacks; (2) absence of intrinsic disease of abdominal and other viscera; and (3) positive evidence of cerebral dysfunction as manifested by a family and, occasionally, a personal history of convulsive disorder, a history of acquired brain damage, abnormal neurologic signs, epileptiform discharges in the electroencephalogram, and a beneficial response to antiepileptic drugs. Electroencephalographic abnormalities are most prominent during sleep and have included discharges of 14- and 6-per-second positive spikes. Dilantin is the most effective agent for the prevention of attacks, and phenobarbital or suppositories of Cafergot are of value in their alleviation.

Paroxysmal headaches, attacks of dizziness, emotional instability, hy-

perkinetic behavior and inappropriate laughter may also occur as manifestations of a seizure disorder.[9, 11] Response to therapy with Dilantin may be dramatic. Phenobarbital is contraindicated in the treatment of hyperkinetic states.

Psychomotor Seizures

These attacks occur less frequently in children than in adults, but an onset before 15 years of age is usual in 20 to 25 per cent of cases.[17, 25] A history of febrile seizures in early childhood is not uncommon.

Psychomotor seizures are characterized by automatic, stereotyped movements, semipurposeful but bizarre patterns of behavior, clouding of consciousness, and a partial amnesia for the event. In the young, repeated swallowing and chewing movements may be the only motor manifestations, but in the older child an arrest or suspension of activity, such as staring or a dazed expression, or an inability to speak, is frequently followed by automatic movements, incoherent or irrelevant speech, rages and temper tantrums. Fears, anxieties or dreamy states are less prominent symptoms, and overactive behavior is more frequent between seizures. A tendency to petit mal and grand mal may also occur. The seizures are sometimes associated with a structural abnormality in the temporal lobe and a focal discharge in the electroencephalogram, but demonstration of a localized lesion is not invariable.

Of drugs which are relatively devoid of serious toxicity, Mysoline is the most effective, but the interseizure disorders of behavior are often refractory to treatment.

Focal Seizures

Focal motor seizures in children frequently have inconstant patterns and may lack the classic progression or "march" of the jacksonian attack. The seizure begins with clonic twitching of one portion of the body, usually the hand or the muscles of the face.[21, 46] Consciousness is retained unless the movements spread to the opposite half of the body and a grand mal seizure ensues. The seizure may be followed by a transient Todd's paresis of the affected limb.

Turning of the head and eyes to one side at the onset of a seizure may indicate a focal lesion in the frontal lobe, usually of the opposite side. Somatosensory disturbances, such as numbness and tingling in a limb, have their origin in the parietal lobe. Visual disturbances are localized in the occipital or temporal lobes. In some instances a structural lesion in the brain cannot be demonstrated, and the focal seizure is associated with a disturbance of cerebral metabolism.

Epilepsia Partialis Continua. Local restricted movements associ-

ated with a focal pattern in the electroencephalogram which occur continuously or intermittently over long periods of time are termed epilepsia partialis continua, or continuing local motor seizures. They may indicate a focus of cortical irritation and are often resistant to drug therapy. Mysoline or phenobarbital may control the seizures, but Dilantin is generally ineffective.

The diagnostic procedures and treatment are determined by the findings on neurologic examination and the course of the underlying disease. In infants and children cerebral tumor and signs of an expanding lesion are uncommon. A nonprogressive structural defect in the brain is a more frequent pathologic finding, and the necessity for surgical intervention is rare.

PROGNOSIS

Since seizures are symptoms of disease, the prognosis is governed principally by the nature of the underlying cause. In patients with seizures of the cryptogenic type the response to treatment is superior, and the incidence of intellectual impairment is lower than in those whose seizures are symptomatic of organic disease of the brain.

Additional factors which are important in the assessment of prognosis include the following: the age at onset of the seizures, the clinical pattern, abnormalities of the electroencephalogram, and the response to therapy. A poor prognosis may be expected if the seizures present at birth, if the clinical pattern is of the infantile spasm or akinetic type, or if the electroencephalogram is diffusely irregular.

Failure to control the seizures may be related to a structural and sometimes degenerative cerebral pathology, but improper management is probably a more frequent explanation. The recognition of contributory etiologic factors amenable to specific corrective measures and the selection of the optimum anticonvulsant therapy[42] may do much to ensure a favorable outcome.

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BACTERIAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

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The present report is based upon the cases of bacterial meningitis which were observed in The Long Island Jewish Hospital from May, 1954, to January, 1960. The current literature has been reviewed so that our data may be compared with available published information.

The subject of meningitis has been treated abundantly in the recent literature.[9, 26] Nevertheless, there are some areas which we believe need further emphasis. In addition to the description of our experiences, we shall endeavor in this report to stress those factors that present specific problems, such as the choice of antibiotic therapy, the use of corticosteroids and corticotropins and discussion of such diverse items as the management of infection caused by organisms not commonly observed in meningitis, mixed infections, and partly treated cases. We will emphasize the clinical differences in the premature infant, the baby and the older child with meningitis.

Tuberculous meningitis will not be discussed.

Description and analysis of our cases will be presented in Tables 12 to 16 followed by brief comments.

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ANALYSIS OF CHARTS

The term "primary" meningitis as used in this report indicates meningitis occurring with other infections, most commonly respiratory. The so-called secondary and mixed infections are those associated with open sinuses such as the dermoid cyst sinus or secondary to operation, particularly for hydrocephalus, meningomyelocele and brain tumor. In general, our findings are in keeping with the experience of others.

Tables 12 and 13 summarize the types of cases encountered.

The various bacteria involved, alone and in combination, in both "primary" and "secondary" meningitis were Hemophilus influenzae 25 times, always "primary"; Diplococcus pneumoniae and Neisseria meningitidis, each twice, always "primary"; Staphylococcus aureus 7 times, twice "primary," 5 "secondary," of which 3 were in combination with other bacteria. Escherichia coli was involved six times, twice "primary," 4 times "secondary," 3 of which were mixed infections. Klebsiella caused meningitis five times "secondarily," 3 times in combination with other bacteria. Proteus occurred twice in "secondary" infections, once mixed. Enterococcus was observed six times, always in mixed infections. Pseudomonas was associated with other bacteria in two instances.

TABLE 12. *Bacterial Meningitis in Children*

	CASES No.	TOTAL %	PRIMARY %	DEATHS No.	DEATHS %
Primary	39	72.2	100	2	5.1
Secondary*	15	27.8	100	7	46.7
Total	54	100		9	16.7
Primary types:					
Hemophilus influenzae†	25	46.2	64.1	1	4.0
Diplococcus pneumoniae	2	3.7	5.1	0	0
Neisseria meningitidis	2	3.7	5.1	0	0
Staphylococcus aureus	2	3.7	5.1	0	0
Escherichia coli	2	3.7	5.1	1	50.0
Unknown	6	11.2	15.5	0	0
Secondary types:					
Escherichia coli	1	1.8	6.7	1	100
Klebsiella	3	5.6	20.0	3	100
Proteus	1	1.9	6.7	0	0
Staphylococcus aureus	2	3.7	13.3	0	0
Mixed infections‡	8	14.8	53.3	3	37.5

* Secondary to operation, central nervous system anomaly, and the like.

† Types determined by positive blood and/or cerebrospinal fluid cultures. Two cases of presumptive H. influenzae meningitis diagnosed by cerebrospinal fluid smear alone.

‡ Includes 2 or more bacteria recovered from cerebrospinal fluid.

Thus H. influenzae was by far the most common of the bacteria encountered. It occurred in 12 infants between 2 months and 2 years; 4 at 2½ years; 2 at 3 years; 3 at 4 years; 2 at 5 years; 1 at 6 years; and 1 at 7 years of age. The cases of D. pneumoniae occurred at 3½ years and at 7 years of age. Neisseria meningitidis occurred at 3 months and at 1½ years. The two cases of "primary" E. coli both occurred in the newborn period. Nine of the "secondary" meningitides occurred before the age of six months. The "secondary" meningitides were associated with operation for central nervous system conditions in all but two cases (Tables 14 and 15).

The age incidence (Table 15) is likewise similar to the common experience; most of the cases occurred within the first three years of life. We did, nevertheless, observe H. influenzae in a somewhat higher percentage of cases (20 per cent) than is commonly reported in the group over 5 years of age. The seasonal occurrence of "primary" meningitis (Table 16) reveals a larger incidence in spring and winter, a total of 28 of the 39 cases occurring during this period. If the six

TABLE 13. *Bacterial Meningitis in Children—Mixed Infections*

BACTERIA	CASES No.	INCIDENCE INDIVIDUAL ORGANISM	FRACTION OF TOTAL CASES
Klebsiella-Enterococcus*	1	Enterococcus	6/8
Pseudomonas-Enterococcus	1	Klebsiella	2/8
Staphylococcus aureus-Enterococcus	1	Pseudomonas	2/8
Staphylococcus aureus-Escherichia coli	1	Staph. aureus	3/8
Pseudomonas-Staphylococcus aureus*	1	E. coli	3/8
Proteus-Escherichia coli-Enterococcus	1	Proteus	1/8
Klebsiella-Enterococcus	1	Total	17/8
Escherichia coli-Enterococcus*	1		

* Expired.

TABLE 14. *Presumptive Predisposing Factors in Secondary Infections of the Central Nervous System*

CONDITION	CASES No.	PRESUMPTIVE MODE OF ENTRY
Hydrocephalus	5	Postoperative infection (4) Lumbar puncture (1)
Meningomyelocele	4	Infected draining sinus (2) Postoperative infection (2)
Congenital dermal sinus:		
lumbosacral	2	Infected sinus tract (2)
occipital	1	Postoperative infection (1)
Brain tumor	1	Postoperative infection (1)
Chronic systemic disease:		
meconium ileus	1	Gastrointestinal tract,
congenital biliary atresia	1	sepsis (2)
Total	15	

TABLE 15. *Age Incidence of Bacterial Meningitis*

	H. INFLUENZAE	D. PNEUMONIAE	N. MENINGITIDIS	STAPH. AUREUS	E. COLI	UNKNOWN	SECONDARY
Premature	0	0	0	0	1*	0	0
0–2 months	0	0	0	0	1	0	5
2–6 months	5†	0	1	0	0	1	4
6–12 months	3	0	0	0	0	0	0
1–2 years	4	0	1	0	0	3	2
2–5 years	8	1	0	1	0	2	3
Above 5 years	5	1	0	1	0	0	1
Totals	25	2	2	2	2	6	15

* Diagnosis made on postmortem examination.
† Only death in this group occurred in youngest infant—i.e. 2 months of age.

TABLE 16. *Seasonal Incidence of Bacterial Meningitis in Children*

	H. INFLUENZAE	OTHER PRIMARY	SECONDARY
Spring:			
March	4	3	0
April	0	2	0
May	4	1	2
Summer:			
June	0	2	2
July	1	0	1
August	1	0	0
Autumn:			
September	1	0	1
October	0	0	3
November	3	3	2
Winter:			
December	4	3	2
January	4	0	1
February	3	0	1
Totals	25	14	15

cases occurring in November were added to this group, only five cases occurred in the months of June through October. This, too, is in keeping with common experience except when dealing with epidemics of meningococcal meningitis.

The case reports which follow have been selected to illustrate special problems of diagnosis and management.

RECURRENT MENINGITIS—DERMOID SINUS

CASE REPORT. D.A., a 19-month-old white male infant, was admitted to the hospital on October 7, 1959, after a 2-day history of temperature to 104° F., stiff neck, vomiting and drowsiness. Lumbar puncture revealed 390 cells, all polymorphonuclears; glucose 60 mg. and protein 69 mg. per 100 ml. Gram-negative rods thought to be H. influenzae were seen on cerebrospinal fluid smear, but the culture remained sterile. Blood and nasopharyngeal cultures were negative. Treatment with sulfadiazine, 100

mg. per kilogram for 7 days, and chloramphenicol, 100 mg. per kilogram for 10 days, resulted in a rapid response, the child becoming alert and responsive after 48 hours and asymptomatic after 5 days. However, he continued to have a temperature of 100 to 100.5° F. daily. Lumbar puncture was not repeated, and the child was discharged after 12 days.

At home he continued to have low-grade fever and irritability for one month without explanation. There was no response to penicillin and erythromycin.

He was readmitted November 19, 1959, because of vomiting, irritability and increased fever for 2 days. On more careful examination a small, flat, 2- by 4-mm. reddish-brown dimpled area was noted in the skin over L 3 to L 4 in the midline. Lumbar puncture revealed 820 cells, 70 per cent lymphocytes, glucose 72 mg. and protein 86 mg. per 100 ml. Blood, cerebrospinal fluid and nasopharyngeal cultures were again negative. Treatment with penicillin, chloramphenicol and sulfisoxazole for 2 weeks resulted in normal cerebrospinal fluid findings and a flat temperature curve. X-ray films of the lumbosacral spine revealed a spina bifida, and at operation an infected dermoid sinus tract extending into the spinal canal was excised. Culture of this material yielded an Enterococcus and Klebsiella. Postoperatively, intravenous chloramphenicol, penicillin in massive doses and nitrofurantoin rendered the child afebrile after 2 weeks. Follow-up 3 months later in February, 1960, revealed the child to be well.

Dermoid sinuses which extend into the central nervous system are frequently associated with recurrent meningitis.[27]

In our series of secondary meningitis dermoid sinuses occurred 3 times out of 15, or 20 per cent. This is much more frequent than we had hitherto been led to believe. In one case a segment of the dermoid cyst which presented on the scalp was mistaken for a wart. In the case described it was overlooked until the second episode of meningitis occurred. Only in the third case was the diagnosis made early, since the sinus was draining and was obviously infected. A similar case with three episodes of meningitis was recently reported by Fisher.[12]

It seems warranted to recommend that a search for such abnormalities be made in all healthy infants and certainly in infants with meningitis, particularly whenever the causative organism is one of those less frequently incriminated, or any bacterium other than H. influenzae, Streptococcus pyogenes, D. pneumoniae and N. meningitidis.

MENINGITIS SECONDARY TO REMOVAL OF DERMOID CYST—CHRONIC BACTEREMIA ASSOCIATED WITH VENTRICULOJUGULAR VALVE

CASE REPORT. R.Z. on admission was a 3-year-old white male infant. In March, 1955, at one year of age, a midline "sebaceous cyst" of the scalp was excised. In August, 1955, he was treated for staphylococcal meningitis at another hospital. A bony defect of the skull in the area of the "cyst" was seen on x-ray examination. He was reoperated on at this time, and a dermoid sinus extending into the cerebellum was excised. His immediate recovery was satisfactory, but in March, 1956, seven months later, progressive hydrocephalus developed. A subarachnoid-peritoneal shunt was performed. The child responded and remained well until July, 1957, when headache, ataxia and a bulging occiput developed (site of 1955 decompression). A right-sided ventriculojugular shunt was performed. The immediate result was good, but on the fourth postoperative day his temperature rose to 102° F. and one week later to 104 to 105° F. without explanation. The fever responded to treatment with penicillin, chloramphenicol and sulfonamides for 3 weeks. Hematuria and a drop in

the white blood cell count to 2000 necessitated discontinuance of the therapy. Abdominal pain and recurrent fever until September led to abdominal exploration. The tube of the subarachnoid-peritoneal shunt was found to be lying free in the abdomen, plugged, and sterile on culture. A few days later a blood culture was positive for Staphylococcus aureus. Nitrofurantoin, oleandomycin and ristocetin, in sequence, were tried, but the bacteremia continued for the next 2 months. Bilateral pneumonia intervened and responded to erythromycin and chloramphenicol, but the bacteremia persisted. Finally, the valve of the ventriculojugular shunt was implicated and removed in November, 1957, after 5 months of bacteremia. Now the infection responded to chloramphenicol. No further shunt procedure was necessary, since the hydrocephalus was arrested. On frequent follow-up examinations in the subsequent 2 years he has remained free of infection. He is slightly ataxic, his head has not grown excessively, and he looks and behaves well.

This case is significant for several reasons. First, it indicates that excision of a midline dermoid cyst of the scalp should not be done except after thorough investigation and then only by a neurosurgeon. Had the skull roentgenogram been done early, the diagnosis would have been made and possibly much of the subsequent illness avoided. Second, the course of the infection suggested subacute bacterial endocarditis, but this could not be demonstrated. A focus for the bacteremia had to be found. The cure after removal of the valve is of interest because the valve was patent and functioning. Yet, at operation, cultures made at all levels of the fascial planes and the valve itself were positive for Staphylococcus aureus. Third, introduction of a ventriculojugular shunt into the opposite side was advised, but fear of recurrence of bacteremia suggested waiting. As often happens, the hydrocephalus was arrested and further operation was avoided.

PROLONGED FEVER AND PLEOCYTOSIS AFTER ADEQUATE THERAPY

Case Report. E.P., a 4½-year-old white female infant, had an upper respiratory tract infection followed 2 days later by shaking chills, lethargy and delirium. Bilateral catarrhal otitis media and rhinopharyngitis were complicated by H. influenzae meningitis. Cerebrospinal fluid revealed 6400 cells, all polymorphonuclears, and an abundance of small, pleomorphic Gram-negative rods which on culture were H. influenzae. Blood and throat cultures were also positive for H. influenzae, but these did not grow well enough for adequate sensitivity studies. Her urine on admission contained 3+ glucose and 4+ acetone and was negative for both after 24 hours.

Therapy consisted of sulfisoxazole, 100 mg. per kilogram, chloramphenicol, 100 mg. per kilogram, and penicillin, 2 million units, intravenously. These were continued for 7 days because of persistent vomiting. The temperature was 104° F. on admission, 102° F. for 3 days. On the fifth day cerebrospinal fluid revealed 1400 white blood cells, with 50 per cent polymorphonuclears, protein 42 mg., and glucose 54 mg. per 100 ml. as compared to 170 mg. and 82 mg. respectively on admission, and a sterile culture. After the seventh day the temperature rose to 100 to 100.5° F. daily. A third lumbar puncture on the fourteenth day revealed 450 cells, all lymphocytes; sugar and protein were normal, and the culture was sterile. Antibiotics were discontinued on the nineteenth day because of the probability that the continued pleocytosis and fever were evidence of reaction to the therapy. The temperature dropped and remained normal.

This case emphasizes the adequacy of 7 to 10 days of therapy after

the cerebrospinal fluid has become sterile. Some felt that these cerebrospinal fluid findings and continued fever were indications for further antibiotic therapy. The decision to discontinue antibiotics was based on the fact that the child was otherwise well clinically.

Continued fever after infection has cleared is often associated with antibiotic therapy. In such a situation this possibility should be considered. Elevated cerebrospinal fluid cell counts are known to occur in some instances after the infection has been eliminated. The prolonged fever, coupled with pleocytosis, suggested a persistent meningitis or possibly a subdural collection of fluid. Since the cerebrospinal fluid was sterile and the patient clinically well, the decision to discontinue therapy after 19 days seemed warranted.

If this child's fontanel had been open, subdural explorations would have been indicated. Yet the course of events shows that subdural collections were not responsible for the continued fever and pleocytosis.

The initial glycosuria and acetonuria are noteworthy. These findings are not rare. In a study made by S.K.[15] 14 per cent of the cases of meningococcal meningitis had transient glycosuria.

MENINGITIS IN A PREMATURE INFANT

CASE REPORT. A.C., a 2 pound 15 ounce male infant, was born after 27 weeks' gestation on March 26, 1957. His condition was fair, but oxygen was required for the first 17 hours of life. Respirations were irregular, 60 to 100 per minute. Color was fair. Breath sounds were clear; heart tones were of good quality with no murmurs present. The abdomen was soft, and the tips of the liver and spleen were palpable. The extremities were edematous. During the first few days of life he had frequent periods of apnea and cyanosis responding to oxygen. Thick yellow mucus was suctioned from the nasopharynx. On the seventh day of life the abdomen became greatly distended. The baby had not passed any stool for 56 hours. Large amounts of yellow fluid were obtained by gastric suction. The extremities were scleremic, the color was poor and the cry weak. The next morning the infant had generalized sclerema; the abdomen became more distended and the respirations irregular. Fecal particles were obtained via gastric aspiration. Chest x-ray showed extensive fibrotic changes involving both lungs, particularly the right side. A flat plate of the abdomen failed to reveal any characteristic distention of the small bowel; however, no gas was seen in the distal colon. The child continued to have increasing periods of apnea and cyanosis. The lungs were clear to auscultation. Five milligrams of cortisone were given intramuscularly for the sclerema, and penicillin 100,000 units daily. However, the baby's condition continued to deteriorate. He expired on April 4 at 9 days of age. Postmortem examination revealed a 920-gm. premature infant with suppurative meningitis due to E. coli, an organizing peritonitis, dilatation of the small and large intestines with impacted stool in the rectum, pulmonary congestion and focal pneumonia.

This patient illustrates the difficulty of diagnosing meningitis in the very small premature infant. His temperature was usually subnormal, 96° F., and never exceeded 98° axillary. Although attention was focused on the abdominal condition, meningitis was not considered seriously. Since intestinal obstruction was suggested, peritoneal infection was con-

sidered, but a volvulus thought more likely. Stiffness of the infant due to the sclerema added to the difficulty of interpretation of the condition and helped to mask whatever neurologic manifestations might have been present. It might be recommended that lumbar puncture be done when a premature infant is regressing without adequate explanation.

FAILURE TO DIAGNOSE EARLY MENINGITIS IN A YOUNG INFANT

CASE REPORT. M.S., a 2-month-old white female infant, had a temperature of 104° F. for 8 days before her hospital admission on May 21, 1956. Physical examination did not reveal adequate explanation for the fever. The next day the temperature rose to 106° F., and the infant had a generalized convulsion lasting 30 seconds. A maculopapular rash was noted over the lower extremities. She was erroneously considered to have roseola, but the fever continued, and the white blood cell count was 31,000 with a shift to the left. S.K. found little to explain the condition except a slightly tense fontanel and a somewhat staring, unhappy facial expression. Antibiotics were recommended, and if the child did not improve, a lumbar puncture was suggested. When it was performed, the cerebrospinal fluid revealed 800 white blood cells, mainly polymorphonuclears. Glucose, 54 mg. and protein, 129 mg. per 100 ml., were noted. The culture was sterile. Treatment with penicillin, sulfadiazine and chloramphenicol resulted in rapid improvement and apparent recovery.

No significant bacteria were recovered from the cerebrospinal fluid, blood or nasopharynx. An electroencephalogram done on March 29, 1956, showed diffuse, symmetrical low to moderate voltage, considered to be slower than usually seen, but perhaps within normal limits. Re-examination in February, 1960, revealed a well child.

Alexander[2] expressed our sentiments very well: "In contrast to the ease with which early meningitis may ordinarily be recognized in the age group just described, infants younger than 7 months often fail to develop the usual signs which lead to the suspicion of meningitis. Special criteria must be used as indications for performing lumbar puncture in order to identify meningitis in its early stages; increased tension of the fontanel, a staring expression, drowsiness alternating with irritability, a high pitched cry, or persistent unexplained fever. The higher mortality in young infants with all varieties of meningitis is explained by the fact that most infants have reached an advanced state of the disease before treatment is applied."

AGRANULOCYTOSIS

CASE REPORT. R.S. was a 2-year-old white male infant with congenital biliary atresia. At 2½ months of age exploratory laparotomy revealed absence of extrahepatic ductal structures. Liver biopsy revealed bile capillary stasis and patchy fibrosis. Hepatomegaly, splenomegaly and ascites were present at one year. He was maintained on bile salts, vitamins and trimeprazine tartrate (Temaril—Smith, Klein and French), 3.75 mg. three times a day, for severe pruritus for the duration of illness. He was hospitalized at 2 years of age because of fever of 4 weeks' duration which did not respond to chloramphenicol therapy. The child presented with pallor, jaundice, massive hepatosplenomegaly, ascites and a questionable stiff neck. Cerebrospinal fluid revealed 224 cells, 90 per cent polymorphonuclears, glucose of 27 mg. and protein of 24 mg. per 100 ml. An Enterococcus was isolated. Blood cultures were repeatedly

sterile. Chloramphenicol, penicillin and sulfisoxazole were given for 2 weeks, at which time the child became afebrile. Pretreatment peripheral white blood cell count was 31,000 with 70 per cent polymorphonuclears. After 2 weeks of antibiotics it was 2000 to 3000 with only 10 per cent polymorphonuclears and thrombocytopenia of 52,000. Antibiotics were discontinued. A bone marrow examination was not remarkable. A week later the white blood cell count had risen to 9000 with a normal differential. The child remained afebrile and well at home for 4 days. On the fifth day his temperature rose to 104° F.; he began to vomit, had a short convulsion and was readmitted to the hospital in coma. Peripheral blood count was 900 white blood cells with 10 per cent polymorphonuclears and 90 per cent lymphocytes and diminished platelets. Despite all measures, the child expired 6 hours after admission after a convulsion. Cerebrospinal fluid culture contained E. coli; blood culture was sterile. Postmortem examination revealed a suppurative meningitis, agenesis of the extrahepatic bile ducts, biliary cirrhosis, hepatosplenomegaly, ascites and jaundice.

This case is presented because of the organisms involved (Enterococcus and E. coli) and because of the possibility that the secondary infection with E. coli may have been associated with the reduction of granulocytes to a total of 200 to 300 per cubic millimeter by chloramphenicol, and possibly Temaril. Escherichia coli meningitis occurs more frequently in newborn and very young infants. It occurs as a secondary invader in such conditions as meningomyelocele, dermoid cyst sinus and complicating conditions treated with antibiotics. In this instance administration of antibiotics resulted in a temporary reduction of granulocytes, thus perhaps predisposing the child to invasion of the blood stream with E. coli.

The chart of antibiotic sensitivities of the bacteria recovered from our patients reveals that only one strain of H. influenzae was resistant to chloramphenicol. The excellent clinical results and the bacteriologic findings make chloramphenicol the drug of choice for this infection.

Although the tetracyclines were as effective in vitro as chloramphenicol, they were not as successful in treatment of H. influenzae meningitis.

The problem of resistance of the Gram-negative rods is borne out in our data. With one exception the failures of therapy were associated with such infections.

It is noteworthy that 9 out of 23, or 39 per cent, of the strains of H. influenzae were susceptible to penicillin. This is similar to data reported.

CHOICE OF ANTIBIOTIC MANAGEMENT OF MENINGITIS: MICROBIOLOGIC ASPECTS

Antibiotics are used in meningitis as in all other infectious diseases to destroy or curtail the offending microorganism. Choice of the antibiotic must be governed by several factors. The type of organism and the etiology of the disease, i.e. primary or secondary, are of the most

TABLE 17. *Antibiotic Susceptibility Pattern of the Bacteria Isolated from Primary and Secondary Meningitis*

	PENICILLIN	STREPTOMYCIN	CHLORTETRACYCLINE	OXYTETRACYCLINE	TETRACYCLINE	CHLORAMPHENICOL	FURADANTIN	NEOMYCIN	NOVOBIOCIN	ERYTHROMYCIN	OLEANDOMYCIN	POLYMYXIN	SULFONAMIDES	TOTAL NUMBER OF BACTERIA
Hemophilus influenzae	9/14	17/6	18/5	21/2	21/2	22/1	22/1	16/7	22/1	16/7	14/9	14/9	9/14	23
Diplococcus pneumoniae	2/0	1/1	2/0	2/0	2/0	2/0	2/0	2/0	2/0	2/0	2/0	2/0	2/0	2
Neisseria meningitidis	3/0	1/2	3/0	2/1	2/1	2/1	3/0	3/0	3/0	3/0	3/0	2/1	3/0	3
Staphylococcus aureus	3/4	2/5	4/3	6/1	5/2	6/1	6/1	6/1	6/1	5/2	4/3	1/6	0/7	7
Escherichia coli	0/6	2/4	4/2	4/2	5/1	5/1	6/0	6/0	2/4	0/6	0/6	3/3	4/2	6
Enterococcus sp.	2/4	1/5	3/3	2/4	2/4	4/2	4/2	1/5	2/4	4/2	3/3	1/5	1/5	6
Klebsiella sp.	0/5	1/4	2/3	2/3	2/3	2/3	2/3	4/1	2/3	0/5	0/5	4/1	2/3	5
Proteus sp.	0/2	1/1	0/2	0/2	1/1	2/0	2/0	0/2	0/2	0/2	0/2	0/2	0/2	2
Pseudomonas aeruginosa	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/0	0/1	0/1	0/1	1/0	0/1	1

Number in upper left half represents sensitive, in lower right half resistant variants as determined by paper disk method.

immediate importance. Both are interrelated, since the causative agents of the so-called primary meningitides are comparatively rare among those organisms which invade the central nervous system consequent to anatomic or surgically created anomalies.

Fortunately the identity, even the presumptive identity, of an organism obtained by examining stained smears of cerebrospinal fluid sediments provides the clue to the choice of antibiotic. There can be no doubt that the final determinant of the antibiotic to be given is the result of microbial susceptibility demonstrated by cultural methods despite its qualitative aspects. But the fulminating and sometimes explosive nature of meningitis demands immediate action. Experience with the available antimicrobials must, therefore, guide the clinician's first measures. Despite the ever-mounting number of chemotherapeutic agents available, the urgency of this disease makes the use of well established agents imperative. It must also be remembered that a considerable number of the newer antibiotics are difficult to transport across host membranes. The blood-brain barrier is indeed one of the most difficult to cross. Thus penicillin will diffuse in limited amounts into the cerebrospinal fluid and in greater amounts when the meninges are acutely inflamed.[13] Chloromycetin similarly appears in low concentration.[32]

The choice of antibiotic is influenced not only by microbial susceptibility and ability to come into contact with its antagonist, but also by the concentration of the agent used and further by the mode of action of the chemotherapeutic agent on the bacterium in its most intimate host environment. Antibiotics must be administered in such dosage as will produce a concentration well above that necessary to kill the offending organism in vitro. Most of the agents used in the treatment of meningitis are eliminated rapidly and in proportion to their concentration by the kidney, detoxified or inactivated by the liver, and diluted by diffusion into organs and tissues. Eagle[11] and many others have suggested that in general a plasma concentration at least four times as high as the sensitivity in vitro of the offending organism should be maintained to achieve therapeutic success. With relatively avascular areas—and the meninges and cerebrospinal fluid must be included in this category—higher concentrations are indicated. Antibiotics will diffuse from the blood into tissues as long as the concentration of the agent in the blood exceeds the level in the tissues. Conditions in the diseased tissue will in the final analysis determine the efficacy of the antibiotic. Many of the antibiotics are affected adversely by the cellular and humoral changes induced by inflammation. Only those which are minimally hindered by such reactions should be used in the treatment of meningitis.

The question of a choice between bactericidal and bacteriostatic

drugs has received considerable attention in clinical discussions. Although bactericidal drugs are commonly preferred, the specter of a Herxheimer reaction or overwhelming intoxication with endotoxins due to massive destruction of bacteria is frequently considered. Although such a reaction is theoretically possible when bactericidal drugs such as penicillin are used, it has been reported only in syphilitic patients.[13] This may be explained by the lower concentration of penicillin achieved in the cerebrospinal fluid, resulting in bacteriostatic rather than bactericidal action of the drug. Although Diplococcus pneumoniae and Streptococcus pyogenes are lysed by very small amounts of penicillin, they exert their disease-producing effects primarily by their numbers, metabolic end products and multiplication rates. Neisseria meningitidis and susceptible Hemophilus influenzae require higher concentrations of the drug and are probably not subject to the bactericidal action of penicillin in the cerebrospinal fluid. Their endotoxins are, therefore, not released in appreciable amounts in response to the presence of this particular antimicrobial.

Adequate levels of bacteriostatic antibiotics suppress multiplication of the offending microorganism, allowing the natural cellular and humoral defenses to dispose of the bacteria present. This consideration engenders insistence that these agents be administered long enough and in adequate amounts. Such a regimen should obviate the possibility that spontaneously resistant mutants among the organisms present will succeed in causing a relapse. The body's defense mechanism should be able to cope with these variants before they can reach disease-producing numbers. It must be remembered, however, that resistance to a given antibiotic by a certain species of bacteria may be based on the capacity of the microorganism to form adaptive enzymes.[1]

Antibiotic therapy of meningitis when no direct bacteriologic evidence is available differs only slightly from that of forms with established etiologic agents. All efforts should be made to obtain circumstantial evidence from nose and throat cultures of the patient and his intimate contacts, particularly in Neisseria and H. influenzae meningitis. Recently, specific antiserums against the commonly encountered causative organisms of "primary" meningitis have again become available commercially. Cerebrospinal fluids which may not yield direct bacteriologic evidence may nevertheless contain the antigens of organisms. Positive precipitin reactions with antiserums can be of great help in selecting the most probable cause in such cases.

When a precise diagnosis of the offending bacterium cannot be made, the age of the child, the presence of a central nervous system abnormality, the presence of an epidemic and the presence of other infections, e.g. skin, lungs, ears, sinuses, should be helpful in determining

TABLE 18. *Antibiotic Treatment—Common Bacterial Meningitis*

AUTHOR	ROUTE	N. MENINGITIDIS		H. INFLUENZAE			D. PNEUMONIAE		
		SD	PEN	CM	SD SM	PEN	PEN	SD	CM
Alexander[3]	IV						5–10x10⁶A		
	IM		P 1x10⁶	100			2x10⁶P		
	PO	200		200	200			200	200
	DAYS	5–7	5–7	10	10				
Amer. Acad. of Ped.[4]	STAT.	50							
	IM		P.1.2–2x10⁶	100			4–12x10⁶A		
							2x10⁶P		100
	S.C.	50–100			100–200			100–200	
	PO	100–250		200	100–300			100–300	200
	DAYS				7				
Bradford[7]	STAT.	50		10–20					
	IV	150		12–20			2–12x10⁶A	150	
	IM		0.6–1.2x10⁶P				1x10⁶P		100
	PO	200		20	200			200	200
	DAYS	5–7	2–3						
Karelitz	STAT.	50						50	
	IV	100	1x10⁶A	100	100	1x10⁶A	2x10⁶A	100	
	IM		1.2x10⁶P			1.2x10⁶P	2x10⁶A		
	PO	200–250		100	200–250			200	
	DAYS	5	5	7	7	7	7–10	7–10	
Krugman and Ward[17]	STAT.	50		100					
	IV	200							
	IM		2x10⁶A						
			1.2x10⁶P				1.2–2x10⁶P		
	PO	200		200	200			200	200
	DAYS	5–7	5–7	7–10	7–10				
Smith[28]	STAT.	100		100					
	IV	100		60–100			3–4x10⁵A		
	IM	100		60–100			3–4x10⁶A	100	
	PO	200		50–100				200	
	DAYS	2							

SD — Sulfadiazine.
PEN — Penicillin.
A — Aqueous Crystalline.
P — Procaine.
CM — Chloramphenicol.
SM — Streptomycin.

All doses are mg./kg./ day except for penicillin, which is expressed in millions of units; i.e. 12.0 x 10^6 = 12 million units.

STAT — Immediately—intravenously.
IV — Intravenously.
IM — Intramuscularly.
SC — Subcutaneously.
PO — Orally.
DAYS — Duration of treatment.

It is usually recommended that the priming dose be given intravenously and that parenteral therapy be continued until patient tolerates oral medication. Penicillin is always given parenterally.

the most likely etiologic agent. If that be decided, the therapeutic indications become reasonably clear.

In any event, the therapy should include an antibiotic which is effective against H. influenzae and Staphylococcus aureus in addition to the effect on D. pneumoniae and beta hemolytic streptococcus. Sulfadiazine, chloramphenicol and penicillin are the drugs we have used in combination when the meningitis has been assumed to be of bacterial origin, not tuberculous or viral.

We have collected the regimens of antibiotic therapy of those authors who have reported extensive experience and have added the regimen we use (Table 18).

MANAGEMENT OF MENINGITIS

Clinical Aspects

Every case of bacterial meningitis is an emergency and requires immediate attention. As soon as the diagnosis is suspected or made, a lumbar puncture should be performed, preferably by someone who has had previous experience, since much depends upon the findings. A smear, preferably of a centrifuged sediment, should be made immediately and stained by Gram's method. This slide should be retained for possible later reference. The fluid should be cultured, glucose and protein determined, and a cell count and differential promptly made.

The physical examination should include careful investigation of the upper and lower respiratory tracts, including the ears and paranasal sinuses. If the child has cervical arthritis or cervical lymph node enlargement resulting in some stiffness of the neck, the presence of central nervous system infection can be eliminated if the neck becomes supple 30 to 60 minutes after a double dose of acetylsalicylic acid. In the many patients treated in this manner we have never observed relaxation of the neck when central nervous system infection was present. The skin should be examined for petechiae, purpura, erythema multiforme, pyoderma, impetigo and sinus tracts along the spine and scalp. The neurologic examination should include the fundi oculi; extensive changes should arouse suspicion of a brain tumor. As is noted in the discussion of manifestations in the infant, the examination must be focused on more subtle changes. A tense fontanel, a staring expression and unexplained fever may be the only signs and symptoms of meningitis. In the premature infant, failure to thrive, sclerema and increasing periods of apnea should indicate the possibility of meningitis. The previously treated person may have limited signs and symptoms such as continued fever, questionable stiff neck, headache, irritability, ocular muscle imbalance, lethargy and anorexia.

Evaluation of the state of circulation and hydration is imperative

Blood is drawn for culture, and electrolytes and continuous intravenous drip of an isotonic solution with added glucose begun. In any type of meningitis, sulfadiazine or sulfisoxazole in the dosage recommended in Table 18 should be started and other antibiotics added in accordance with indications. If the clinical indications are those of a meningococcal meningitis, sulfadiazine suffices, but many prefer to add penicillin. If the patient is a premature or a very young infant, there is the likelihood that Staphylococcus aureus or E. coli is the causative agent. Chloramphenicol should be added to sulfadiazine and penicillin and these drugs given simultaneously and continued until culture and sensitivity studies indicate either continuation or change to more effective drugs. If the child is between two months and five years of age, H. influenzae, D. pneumoniae or Streptococcus pyogenes should be suspected. In these instances it is the custom of many to introduce three drugs, sulfadiazine, chloramphenicol and penicillin, until the bacteriologic results are known. In cases of pneumococcal or streptococcal meningitis, chloramphenicol is unnecessary. The dosage of penicillin may have to be increased when the infection is pneumococcal. The same combination of drugs, penicillin, sulfadiazine and chloramphenicol, should be used in all incompletely treated cases.[16] If H. influenzae is found, two variations in treatment are recommended. Because this organism is frequently resistant to penicillin and because penicillin does not readily pass the blood-brain barrier, it is not included by most authors. Streptomycin is sometimes substituted for or added to chloramphenicol therapy. We have continued to recommend penicillin for two reasons because many of the strains isolated are sensitive to penicillin, and secondly, of these, some are resistant to Chloromycetin.

In cases of the less common invaders of the meninges, antibiotic therapy must be adjusted to the known bacterial sensitivities of the organism in question. Thus even drugs known to be nephrotoxic and neurotoxic should be given when the risk of failure to cure is greater than the possible damage resulting from the antibiotic. Obviously, the least toxic agents likely to overcome this infection should be given by any and all routes, including the intrathecal. The more toxic agents under consideration are bacitracin, polymyxin B, kanamycin, vancomycin, ristocetin and neomycin. Polymyxin 2.5 mg. per kilogram per day intramuscularly or a total of 2.5 mg. per day intrathecally and bacitracin 5000 to 10,000 units daily intrathecally have been successful.[8]

If the circulation is poor, blood or plasma and Neo-Synephrine may be of help.

Fluids and electrolytes should be provided in adequate amounts to prevent the hypoelectrolytemia, particularly the hyponatremia, which often occurs.[23] The patient should be kept comfortably warm and observed constantly. Measures for treatment of convulsions should be

at hand and oxygen supplied routinely. Antibiotic therapy should be given parenterally until such time as the patient accepts and retains fluid orally. The duration of treatment varies somewhat with the individual therapist. All agree that meningococcal disease requires a shorter period of therapy than do the other primary infections and that the "secondary" meningitides must be treated until both the meningitis is cured and the primary condition eliminated. With prolonged antibiotic therapy one must be cognizant of the possibility of reaction to the drugs in the form of fever and skin eruptions. Clinical progress of the patient and sterile cerebrospinal fluid should enable one to arrive at the decision to continue or discontinue therapy.

The use of corticosteroids and corticotropins has been left out deliberately, since we shall discuss this subject in considerable detail in the subsequent section.

Corticotropins and Corticosteroids in Treatment of Severe Infection

The corticotropins and adrenal corticosteroids (Table 19) had been introduced in the management of meningitis, particularly in those forms accompanying fulminating meningococcal bacteremia[14] (Waterhouse-Friderichsen syndrome). It was believed that with the damage to the adrenal gland either because of hemorrhage or areas of cellular degeneration, corticosteroids were not produced in necessary amounts and that the collapse of the patient was associated with adrenal insufficiency. In a recent publication May[22] indicated that the shock which occurred in fulminating infections such as in the Waterhouse-Friderichsen syndrome was caused by the bacterial endotoxins. He also brought forth evidence indicating that the adrenal gland was capable of responding to stimulation by the corticotropins and that the output of corticosteroids was increased to levels above normal. The danger of augmenting the effect of the endotoxins through a mechanism distinct from the generalized Schwartzman phenomena as described by Thomas[30] was likewise mentioned. For these reasons as well as a lack of evidence in the literature of benefits derived from the use of steroids in the management of severe infections, May concludes that these drugs are of no beneficial effect in diseases produced by bacterial endotoxins. He further states that because of the danger of increase of endotoxin effect, they are contraindicated.

Applebaum and Abler[5, 6] report 10 deaths in 28 patients with Waterhouse-Friderichsen syndrome treated with hydrocortisone 100 to 200 mg. per day administered intravenously for the first day and cortisone 200 to 300 mg. per day for 5 days. Ribble and Braude[25] had a survival of 11 out of 12 patients with D. pneumoniae meningitis treated with ACTH, cortisone and hydrocortisone. The largest series of cases is that

TABLE 19. *Corticotropin and Corticosteroid Treatment of Bacterial Meningitis*

AUTHOR	N. MENINGITIDIS		D. PNEUMONIAE		H. INFLUENZAE		STEROID			
	Yes	No	Yes	No	Yes	No	Type	Dose	Route	Levophed
Applebaum and Abler[5, 6]	18/28WF						Hydro Cort	100–200 200–300	IV	
Ribble and Braude[25]			11/12				ACTH Hydro Cort	10–160 50–150 50–150	IV	No
Lepper and Spies[18]	22/22 27/27 0/5		10/11 11/12		28/28 29/29		Hydro ACTH	250 1 mg/kg.	IV IM	Yes

Numerator represents survivors.
Denominator represents total number of patients.
WF—Waterhouse-Friderichsen syndrome.
All doses are mg./day except where indicated.
ACTH expressed as units/day.
Hydro—Hydrocortisone.
Yes—Steroids given.
No—No steroids given.

of Lepper and Spies,[18] who had 22 consecutive recoveries of patients with meningococcal meningitis treated with steroids. They also had 27 recoveries out of 27 patients not treated with steroids. The five patients with Waterhouse-Friderichsen syndrome treated with steroids all succumbed.

In meningitis caused by D. pneumoniae 10 of 11 treated survived, as did 11 of 12 patients not treated with steroids. Of the 57 cases of H. influenzae observed, 28 treated patients survived, as did 29 who did not receive steroids. These data seem to be fairly convincing of the failure of corticotropin and corticosteroid in the doses given to increase the chance of survival. Our own experience is too limited for personal opinions, but because of the absence of convincing data in the literature and because of the arguments promulgated by May,[22] we too feel that severe infection is not an indication for the use of these drugs.

In Table 20 the reported experience with corticotropins and corticosteroids in therapy of meningitis is reviewed. Case reports and papers reporting very few cases have not been included.

ACUTE SUBDURAL EFFUSIONS COMPLICATING BACTERIAL MENINGITIS

The question of the incidence and exploration for subdural effusion has been the subject of considerable discussion and, as will be seen, is not yet solved.

In 1950 Smith[29] and McKay et al.[20] called attention to the occur-

rence of subdural effusions, particularly in infants and more frequently if these infants had not been treated in the first 48 hours of disease. The incidence of this complication varies considerably among different authors, ranging from none in Desmit's[10] 114 cases and none in Watson's[31] 45 cases to 33 per cent in the 23 patients of McKay et al.[21] and 46 per cent in Smith's[29] series of 43 patients. In a more recent survey of 292 cases Platou[24] reports an incidence of 16 per cent. In our experience with 54 cases only 2 subdural collections were found of the 4 investigated for the possibility.

Subdural collections may occur at any age, but are most frequently encountered below the age of one year. McKay[19] reports that 60 per cent and Smith[29] 50 per cent of all patients under one year with bacterial meningitis had this complication. Fifty of 55 (91 per cent) of Platou's[19] patients with proved collections were under one year of age, and 38 of 55 (68 per cent) were less than 6 months. Yet Watson[31] reported no effusions in his 45 cases of neonatal meningitis.

No demonstrable relation between sex and race can be established as predisposing to the formation of subdural collections. The multiplicity of theories advanced suggests that the etiology for the formation of subdural collections is not yet clearly established.

Less than 1 ml. of clear fluid is normally obtained by puncture of the subdural space. Any amount over 1 ml. is considered significant. Typical subdural collections are xanthochromic, cloudy and often blood-tinged. Occasionally frank pus may be encountered. The fluid is usually sterile, but cultures should always be done. Incidentally, this is sometimes the only method of establishing a positive bacteriologic diagnosis in cases of unknown etiology, but this procedure is not recommended for this purpose. Collections may be unilateral or bilateral, but the presence of fluid on one side does not obviate the necessity for a tap on the opposite side. Protein may be elevated even in excess of 1 per cent, and pressure is usually elevated. Most effusions will be found on the initial tap, but in some cases a second or even third tap may be necessary to establish the diagnosis.

Although the incidence of subdural effusions is high in the first year of life, routine investigation of the subdural space is not warranted. Subdural effusion may be caused by the procedure itself. But clinical signs and symptoms persisting beyond the ordinarily expected period should raise the question of subdural collection. Among these signs and symptoms are persistent fever, vomiting, opisthotonos, rapidly enlarging head, recurrent or persistent bulging fontanel, convulsions during convalescence and focal neurologic signs. All these raise the suspicion of a subdural effusion and require a diagnostic tap in infants with open fontanels.

This procedure in an older child would require burr holes, and this

has been an obvious deterrent. The paucity of available data as to the incidence in older children, and the disappearance of suspicious signs and symptoms with continued antibiotic therapy suggest either decreased incidence, absorption of the exudate under continued therapy or the possibility that the clinical manifestations were in fact due to other than subdural fluid.

The natural course of this condition is obscure, and the best management must await further controlled studies. Most observers recognize the need for active treatment, however, and recommend repeated aspiration every one to two days in an effort to drain the collection. If, after repeated aspirations in the course of two to three weeks, the fluid shows no sign of regression, surgical exploration with removal of membranes is often recommended. McKay et al.[19] feel that earlier surgical intervention is warranted, since at time of operation 34 of 40 patients had already developed membranes 7 to 10 days after discovery of the collection. Follow-up studies appear to indicate an improved prognosis with earlier operation in their series. If repeated taps yield increased amounts of fluid with successively larger amounts of blood sediment, trauma resulting from the taps must be carefully weighed against the possible damage from leaving the accumulated fluid.

Sequelae, such as epilepsy, mental retardation, hydrocephalus, are reported to be more common among those children who develop subdural collection.[24] The incidence appears less in older children, but a subdural collection when present is an ominous prognostic sign in terms of more consistent association with later handicaps. One cannot, however, predict severity or number of residua from the amount, time of discovery, nature or duration of the collection. The association of effusions with later sequelae is commonest in the younger patients and in those who were treated late, but this may reflect severity of the disease rather than a causal relationship, although central nervous system damage from a subdural collection is well documented.

SUMMARY

In summary, we have described our experience in 54 cases of acute bacterial meningitis in infants and children. Most of the "primary" cases were due to Hemophilus influenzae. These occurred in children from two months to seven years of age, most often in those under four years of age. In all probability these infections were secondary to upper respiratory tract infections, including otitis media and acute sinusitis. Meningococcal meningitis occurred infrequently, a fact which may be explained by the absence of epidemics in the area during this period. Streptococcal meningitis has practically disappeared since the use of antibiotics in the management of the streptococcoses.

Of singular importance has been our experience with the "secondary" meningitides, particularly those associated with dermoid cyst sinuses. In such cases one must be particularly careful to eradicate the focus of infection, the dermoid cyst itself, if recurrence of the meningitis is to be avoided. These infections are caused by the bacteria less commonly encountered. such as Enterococcus, Proteus, Klebsiella, Pseudomonas, E. coli and Staphylococcus aureus occurring individually, often in combination. The frequency of shunting operations for hydrocephalus has increased the cases of "secondary" meningitis. In these instances the most common organism is Staphylococcus aureus. In one instance it produced a picture very much like subacute bacterial endocarditis. It was necessary to remove the child's valve before it became possible to eradicate the infection.

Attention has once more been called to the difference in clinical manifestations of bacterial meningitis in the premature and in the very young infant as compared to the older child.

The use of corticosteroids and corticotropin has been discussed and the literature reviewed, and our conclusion that they are not indicated seems warranted on the basis of the evidence presented.

The various forms of therapy used have been reviewed, outlined and commented upon. The difference between the various regimens is not great, and the results are comparable. This would indicate that one may choose almost any one of the regimens of therapy and attain good results.

The question of the subdural collection and what to do about it is still unanswered for the older children. The likelihood that subdural collections primarily occur in infants and much less frequently in older children seems probable. This would have to be so to justify the relative infrequency of exploration of the subdural space in older children with meningitis.

Finally, it is most important that meningitis be considered an emergency and that treatment be instituted at the first possible moment. The philosophy of treating acute bacterial infections suspected of being meningitis with antibiotics can be defended, even though early treatment may eliminate positive identifying signs and symptoms and make accurate bacterial diagnosis difficult. It probably lessens the intensity of the disease and perhaps prevents more serious damage.

A questionnaire was sent out to each doctor who admitted a child to The Long Island Jewish Hospital for treatment of meningitis. We were anxious to know whether the follow-up revealed any sequelae. The response has been amazing. With the exception of a few children who moved from their original locations there has been only one out of 19 responses which indicates complications. This most astonishing result suggests either that the results of the management of meningitis are

much superior to what they were in the past or that the follow-up is not adequate. More detailed investigation is necessary in order to draw definite conclusions.

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HEREDITARY METABOLIC DISORDERS INVOLVING THE NERVOUS SYSTEM

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The concept of "inborn errors of metabolism" was first suggested by Sir Archibald Garrod in 1908. In the Croonian Lectures at the Royal College of Physicians he suggested that four metabolic disorders—albinism, alkaptonuria, cystinuria and pentosuria—have certain features in common. First, in all four conditions the onset of the particular abnormality could be dated to the first days or weeks of life, especially when a special effort was made to do so. The second characteristic was that the conditions were relatively benign and compatible with normal life-expectancy. The third characteristic was their familial occurrence in a considerable number of cases. A fourth feature noted by other clinicians in his day was the frequency with which these disorders occurred among the offspring of consanguineous marriages.

Half a century later rapid progress in the basic sciences has given body and substance to what was, by necessity, supposition in Garrod's time. The original four inborn errors of metabolism have now been increased to well over one hundred. We now know not only how these

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conditions are transmitted from one generation to another, but also some of the various biochemical processes responsible for these changes.

SOME CONCEPTS OF INBORN ERRORS OF METABOLISM

In a consideration of the hereditary metabolic disorders involving the nervous system it is pertinent to start off by considering three basic problems which concern all inborn errors of metabolism: (1) How do they arise? (2) How are they transmitted? (3) How is the abnormality expressed in the affected person?

It has been well established that all of us are endowed with chromosomes, small bodies of various sizes and shapes located in the cell nuclei. With few exceptions every cell in the human body contains 23 pairs of chromosomes, one member of each pair being derived from the father and the other member from the mother. The gene is a submicroscopic substance of the chromosome which determines the inheritable characteristics of an organism. For instance, there is a gene which determines the character of the MN blood groups; another that determines whether a person will have thalassemia; and yet a third that determines whether he will show homogentisic acid in the urine; and so on. Suitable experiments have shown that the genes are arranged in a linear sequence along the length of the chromosomes and that the sequence tends to be the same for all persons of a particular species. During fertilization the father contributes one of each pair of each of his chromosomes, and the mother contributes one of each pair of her chromosomes, and these two make up the pair of chromosomes in their offspring. Since the genes are located along the length of the chromosome, usually there is for each gene on a maternal chromosome a corresponding homologous gene on the paternal chromosome in the same position. Most of the time the two homologous genes are identical and of the type most common to the species—and that is "normal" as we say. For example, most of us have the normal form of the gene for galactosemia, and therefore we have normal quantities of galactose-l-phosphate uridyl transferase in our red cells. But, here and there along the line of genes on a chromosome, there is likely to be found an abnormal, or as we say a "mutant," gene. If this should occur in the gene for galactosemia, the person carrying the abnormal gene would have approximately half of the normal levels of this enzyme in his red cells; and if both genes in that position should be abnormal, the patient would have little or no enzyme activity. All the inborn errors of metabolism are the results of mutation of one or another of the genes.

The exact reason why a normal gene becomes a mutant gene is not known. Investigators have suggested that environmental factors, such as temperature, atmospheric oxygen, and nutrition, may play a role.

There is considerable evidence that radiation from x-rays and ultraviolet light can cause fresh mutations. Regardless of the cause, once a mutation occurs, the abnormal characteristics will be transmitted from one generation to another. Classically, a genetic defect can be transmitted by one of three modes: dominant, recessive or sex-linked. Most of the hereditary disorders involving the central nervous system are transmitted by a recessive gene, such as the one for galactosemia. If, as shown in Figure 38(*a*), one of the parents is a heterozygote and the other is completely normal, half of the offspring will be heterozygotes and the other half will be completely normal. Since the condition is a recessive one, the heterozygote cannot usually be identified by simple means, and the abnormal gene is passed from one generation to another without the condition being known.

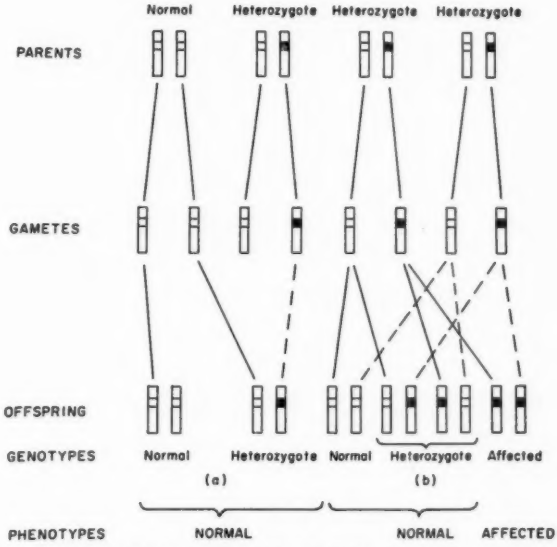

Fig. 38. Recessive mode of inheritance. (After D.Y.-Y. Hsia: *Inborn Errors of Metabolism*. Year Book Publishers, Inc.)

When two such heterozygotes mate, a rather different picture emerges, as shown in Figure 38(*b*). Each of the heterozygotes will contribute one normal and one abnormal gene at the gamete stage. Three types of offspring will result. One quarter of them will receive one normal gene from the father and a similar normal gene from the mother and will be completely normal, in the genetic sense. One half of the offspring will receive one normal and one abnormal gene from each of the parents and will be heterozygotes, just like their parents.

The final quarter of the offspring will receive one abnormal gene from the father and one abnormal gene from the mother; they will be homozygotes with two abnormal genes for the trait and will have the full-blown clinical picture of galactosemia.

Finally, let us discuss how a gene acts. Although we know a good deal of how a gene determines the inherited characteristics for an organism, we know relatively little about its physical or chemical properties, and even less about how genes reproduce and act inside the body. Careful studies have shown that a gene is a submicroscopic particle made up of desoxyribose nucleic acid and protein. Although genes cannot be seen on human chromosomes, they have been localized on the fruitfly chromosome, and there is little doubt that they exist as physical entities. The mode of action of the small particles is not known. One theory is that they act as a model consisting of standard residues, nucleotides, amino acids and perhaps other prosthetic groups and are copied by another chain. Another theory is that the gene and the whole chromosome are "copied" into a completely different structure, much like antigens with an antibody. The "template" or "negative" is again copied, giving two new positions, and so on. Since vast numbers of

TABLE 20. *Inborn Errors of Metabolism Causing Neurologic Disorders*

	MENTAL DEFICIENCY	NEUROLOGIC DISORDERS	CONVULSIONS
Disorders of protein metabolism:			
Phenylketonuria	+		+
Maple sugar urine disease	?	+	
Hartnup's disease	+	+	
Cystathioninuria	+		
Argininosuccinic aciduria	+		+
Leucine sensitivity			+
Wilson's disease	?	+	+
Disorders of carbohydrate metabolism:			
Galactosemia	+		+
Glycogen storage disease		+	+
Disorders of lipid metabolism:			
Gaucher's disease (infantile form)		+	
Niemann-Pick disease	+		
Amaurotic family idiocy	+	+	
Gargoylism	+	+	+
Miscellaneous:			
Congenital nonhemolytic jaundice with kernicterus	+	+	
Deficiency of pseudocholinesterase		+	
Hereditary periodic paralysis		+	
Hyperkalemic familial periodic paralysis		+	
Familial cretinism with goiter	+	+	

molecules have to be created each day to replace those which degenerate and disappear, it is apparent that one copying process would probably not be sufficient to do the job. Instead, several such processes must go on in separate stages, and we are observing only the end-results of this mechanism.

Although we know relatively little about gene reproduction, we do know a good deal about the primary effect which a gene exerts upon specific molecules in the body. The primary gene effect represents the first direct result of the action of the gene which can be shown by physical or chemical means. We can illustrate this by considering phenylketonuria. We know from genetic studies that, when the gene for phenylketonuria is present in the abnormal form, the enzyme phenylalanine hydroxylase is inactive. This in turn causes accumulation of phenylalanine in the blood, excretion of phenylpyruvic acid in the urine, and certain effects upon the central nervous system and upon pigment production. In the laboratory we cannot identify the exact genes which bring about this abnormality. But by means of chemical and physical studies we are able to demonstrate the effect of the gene in the patient himself.

A list of the "inborn errors of metabolism" causing neurologic disorders is given in Table 20. These will be discussed in terms of disorders associated with (1) protein metabolism, (2) carbohydrate metabolism, (3) lipid metabolism, and (4) miscellaneous conditions.

DISORDERS ASSOCIATED WITH PROTEIN METABOLISM

PHENYLKETONURIA

Since Folling[14] first described phenylketonuria in 1934, it has been found that about 1 per cent of the mental defectives in state institutions in the United States are suffering from this condition.

Clinical Features

Phenylketonuric children appear to be quite normal at birth. Between three and six weeks phenylpyruvic acid can be detected in the urine, and the child fails to develop mentally at the normal rate. In early childhood the children have an attractive appearance with nearly normal stature and head size. Characteristically, they are blond with blue eyes and fair skin. They tend to suffer from eczema.

Neurologically, phenylketonurics show no paralysis and no changes in muscle tone, though there is accentuation of both superficial and deep tendon reflexes. Electroencephalography shows some abnormal features such as a long RSP complex with multiple seizure foci, and convulsions sometimes occur. The majority of patients have an I.Q. of 30 or less,[27] but a few high-grade cases with near-normal intelligence have been described.

Pathogenesis

Phenylketonuria is caused by a deficiency of *phenylalanine hydroxylase*, the liver enzyme which converts phenylalanine to tyrosine.[28] This results in excessive accumulation of l-phenylalanine in the blood and cerebrospinal fluid. This in turn causes three kinds of effects (Fig. 39). (1) The excessive phenylalanine is converted, by transaminase, to phenylpyruvic acid. This in turn is converted to phenyllactic acid,

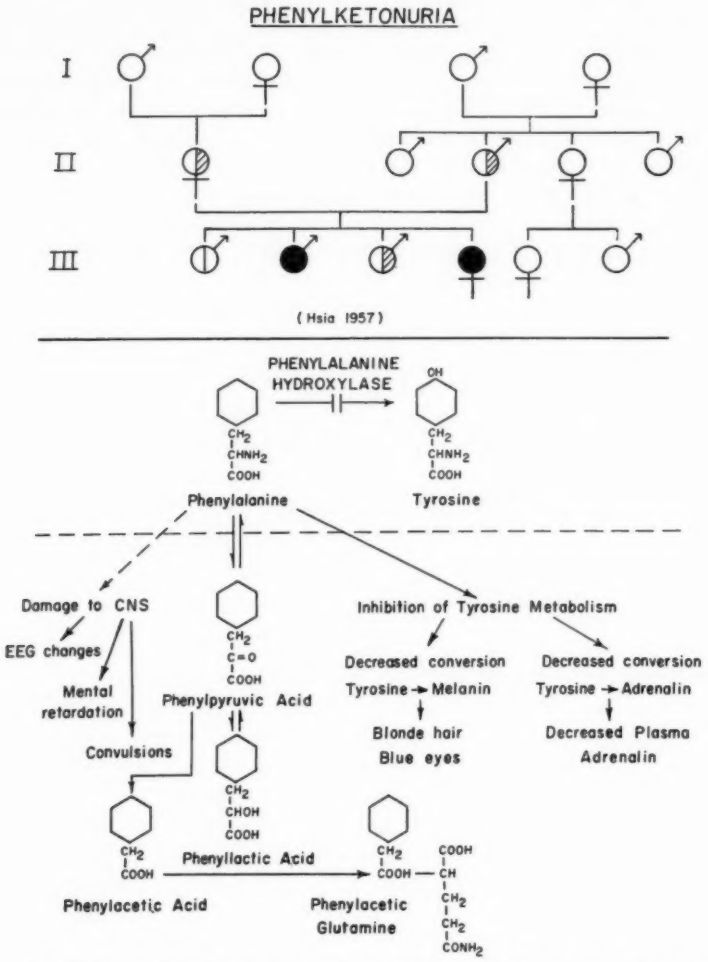

Fig. 39. Pathogenesis of phenylketonuria. (After D.Y.-Y. Hsia: *Inborn Errors of Metabolism*. Year Book Publishers, Inc.)

phenylacetic acid and phenylacetylglutamine and excreted in the urine. For reasons which are still obscure, o-hydroxy-phenylacetic acid, m-hydroxy phenylacetic acid, and indole products derived from tyrosine, and tryptophan are also seen in the urine of such patients. (2) The excessive phenylalanine also inhibits the normal pathways of tyrosine metabolism. There is a decreased production of melanin, and this is responsible for the light pigment in the skin and hair of such patients.[10] There is also a disturbance in epinephrine production, since phenylketonurics have unusually low blood epinephrine levels. (3) The excessive phenylalanine or one of its products probably causes some, as yet unexplained, damage to the central nervous system; this is characterized by mental retardation, epileptic seizures and abnormal electroencephalogram changes.

Inheritance

Phenylketonuria arises once in every 40,000 births in the United States and is transmitted by an autosomal recessive gene. In this situation, if a given family has one affected child, the chance of another case occurring in a subsequent pregnancy is 1 in 4, or 25 per cent.

The heterozygous carriers of phenylketonuric genes may be identified by means of phenylalanine tolerance tests,[20] in which 0.1 gm. per kilogram of l-phenylalanine is administered by mouth after an overnight fast, and plasma phenylalanine levels are determined 1, 2 and 4 hours after the test dose. As a general rule, heterozygous persons have levels twice as high as those seen in normal controls.

Diagnosis

The diagnosis of phenylketonuria may be made by showing the presence of phenylpyruvic acid in the urine by one of three ways:

Direct Testing of Urine. A few drops of 10 per cent ferric chloride are added to a specimen of urine previously acidified with a few drops of 1NHCl. If phenylpyruvic acid is present, the urine will turn an intense green color. This test should be done on relatively fresh urine, since false negatives sometimes occur if the specimen is allowed to stand in a warm room for several hours.

Diaper Test. A diaper with freshly voided urine may be tested in the same manner first by acidification and then by the addition of a few drops of 10 per cent ferric chloride. An intense green color is noted on the diaper if phenylpyruvic acid is present.

Filter Paper Tests. The urine may be impregnated on a piece of filter paper and dried. The paper will turn bright green on the addition of ferric chloride if phenylpyruvic acid is present. Previously impregnated filter paper is also available commercially and when dipped into urine or on a wet diaper will turn bright green when phenylpyruvic acid is present (Manufactured as Phenistix by Ames Co., Elkhart, Indiana).

The diagnosis should be confirmed by demonstrating an increase of l-phenylalanine levels in the plasma. A number of different methods are

available for measuring phenylalanine levels in the blood. In our experience the modified phenylalanine decarboxylase method* has been most satisfactory. In normal fasting persons the plasma phenylalanine level is between 1.0 and 1.5 mg. per 100 ml. In untreated phenylketonurics levels of 15 to 50 mg. are seen.

In a phenylketonuric infant these tests become positive from four to six weeks of age.[3] Screening should therefore be done on the occasion of the first well-baby check-up.

Treatment

All the biochemical abnormalities associated with phenylketonuria can be corrected or eliminated by the use of a low phenylalanine diet[5] (Fig. 40) which is made up of a number of components:

Low-phenylalanine protein hydrolysate is available in the form of (1) Lofenalac (manufactured by Mead Johnson & Company, Evansville, Indiana). One half cup of Lofenalac daily is required to supply 50 calories per pound of body weight. By about 1 year of age 1½ cups are needed, and by about 3 years of age 2½ to 4 cups are needed daily. The formula is made up by measuring 1 packed level measuring scoop of Lofenalac for each 2 ounces of water, and no other supplements are

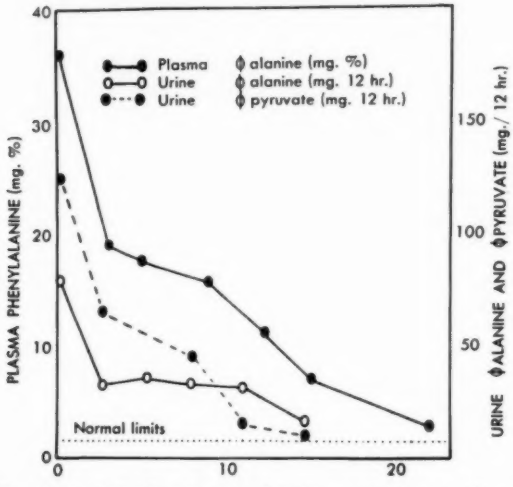

Fig. 40. The effect of diet low in phenylalanine content upon phenylalanine and phenylpyruvate levels in phenylketonuria. (After D.Y.-Y. Hsia: Recent Advances in Human Genetics. *Postgrad. Med.*, 22:203, 1957.)

* This method is described in detail in reference 21. The decarboxylase may be obtained commercially from the Nutritional Biochemicals Co., Cleveland, Ohio, under the name "Tyrosine decarboxylase."

required in the formula. (2) Ketonil (manufactured by Merck & Company, Inc., Rahway, N. J.). In a younger infant the formula is made up by taking 3 tablespoonfuls of Ketonil, 9 tablespoonfuls of Dextri-Maltose, 2 ounces of Lipomul (manufactured by Upjohn Company, Kalamazoo, Michigan), flavoring, and water to make up 24 ounces. In an older child this is made up by taking 6 tablespoonfuls of Ketonil, 10 tablespoonfuls of cane sugar, 2 ounces of Lipomul, flavoring, and water to make up 24 ounces.

One per cent protein fruits and vegetables. These include apples, bananas, blueberries, cabbage, cantalope, carrots, celery, cherries, cranberries, cucumber, grapefruit, onions, oranges, peaches, pineapples, plums, radishes, raspberries, squash, strawberries, tangerines, tomatoes, turnips and watermelon. Between ½ and 1 cup daily is permissible. Mead Johnson & Company have made out a table of "phenylalanine-equivalents."[40] These are in general acceptable except for the equivalents of cereals.

Cereals. Tapioca and corn starch are the only two acceptable cereals with sufficiently low phenylalanine content.

Sugar and butter should be used liberally.

Multivitamin and ferrous sulfate supplements.

All patients should be seen at least once every 6 weeks, and the plasma phenylalanine level should be kept below 3 mg. per 100 ml. The phenylpyruvic acid excretion cannot be used as a measure of biochemical control, since it disappears from the urine when the plasma phenylalanine levels fall below 10 mg.[21]

Results. The results of low-phenylalanine treatment in eight phenylketonuric children from our Clinic are summarized in Table 21. All are healthy but small and underweight (Figs. 41, 42). These cases were followed by careful biochemical testing at regular intervals, and the present level of intellectual achievement, with one exception, was performed by one psychologist.

In the literature, a total of 37 additional younger children have been treated with the diet and followed up reasonably closely with biochemical determinations. These, together with the results, are summarized in Table 22.

The value of a low phenylalanine diet in phenylketonuria is as yet difficult to evaluate. The data which have been collected point tentatively to these conclusions: (1) Treated children have a much better chance of avoiding severe mental retardation than do untreated. (2) Children whose treatment is initiated before the age of six months and in whom good biochemical control has been achieved have an excellent chance of avoiding severe retardation (I.Q. below 50) and will probably fall into the borderline to normal range of intelligence (70 to more than 100). (3) Children whose treatment is begun between 7 and 18

TABLE 21. *Results of Low Phenylalanine Diet upon Phenylketonuric Children*

PATIENTS	DATE OF BIRTH	FAMILY HISTORY	PRESENTING CLINICAL FEATURES					DIETARY THERAPY		PRESENT INTELLIGENCE	
			Age at Diagnosis	Retardations	Convulsions	Eczema	Fair Hair & Eyes	Duration	Biochem. Control*	Age of Testing	I.Q. Score†
B.Z.	June, 1958	+	2/12	—	—	+	+	1–5/12	Fair	1–6/12	67
D.B.	May, 1958	—	5/12	±	—	+	+	1–6/12	Excellent	1–4/12	69
B.W.	Jan., 1958	+	4/12	—	—	—	+	2	Excellent	1–9/12	36
G.C.	Sept., 1955	+	7/12	+	—	+	+	3	Fair	4—6/12	Low
C.J.	Aug., 1955	+	1–11/12	+	—	—	+	2–6/12	Excellent	4–5/12	17
E.W.	April, 1956	+	2	+	—	—	+	1–6/12	Excellent	3–6/12	39
J.C.	Jan., 1956	+	2	+	+	—	—	1	Fair	2–11/12	30
M.M.	Aug., 1954	—	5	+	—	—	+	6/12	Excellent	5—2/12	58

* Excellent biochemical control indicates a consistent plasma phenylalanine level of 3 mg. or less.
Fair biochemical control indicates a plasma phenylalanine level between 3 and 8 mg. per 100 ml.

† All the tests were performed by the same psychologist using the Cattell Infant Intelligence Scale.

months of age have a good chance of achieving the status of educable mentally handicapped children (I.Q. 50 to 70). (4) If the diet is initiated between 19 and 36 months, the chances of achieving this educable level are just fair. (5) If treatment is not begun until after the second birthday, the child is likely to be retarded beyond even the trainable threshold (I.Q. 30).

The validity of these conclusions must be questioned until (1) many more new cases are studied and (2) the present cases have been fol-

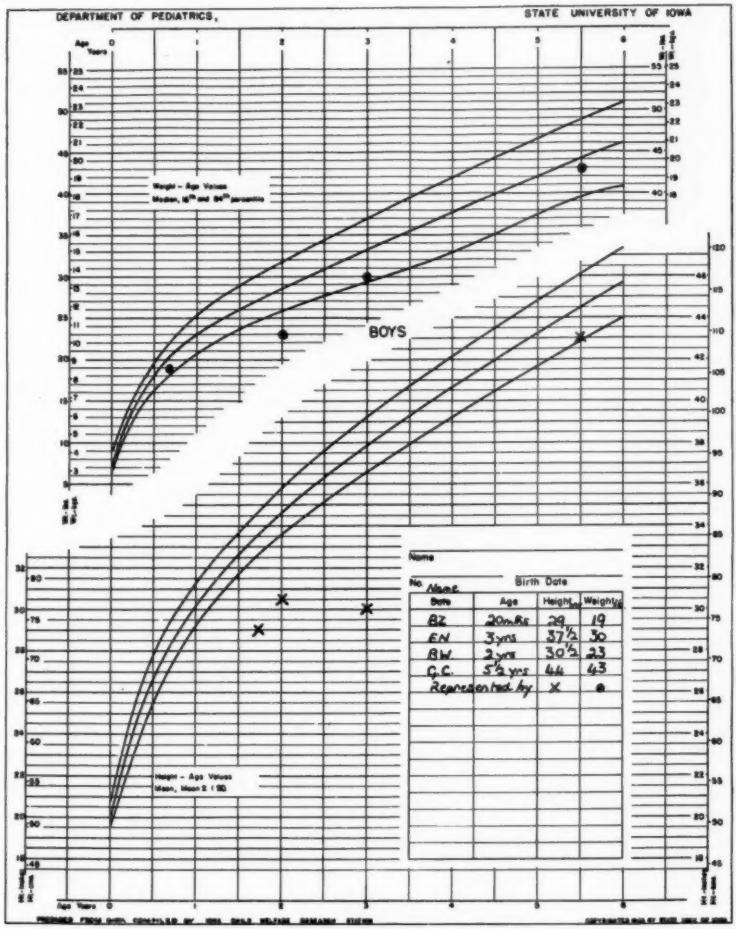

Fig. 41. Height and weight of boys on low phenylalanine diet.

lowed up for several more years. There are some cogent reasons for caution in this matter. The number of cases observed is still too small to yield a smooth I.Q. distribution. (One example of a result which deviates from the general trend is that 3 out of 7 children started on diets between the ages of 4 and 5 are doing relatively well with I.Q.'s between 60 and 69.) Another consideration is that tests of infant intelligence, though of proved reliability, have also been shown for normal populations (I.Q. 70 to 130) not to be predictive of intellectual status

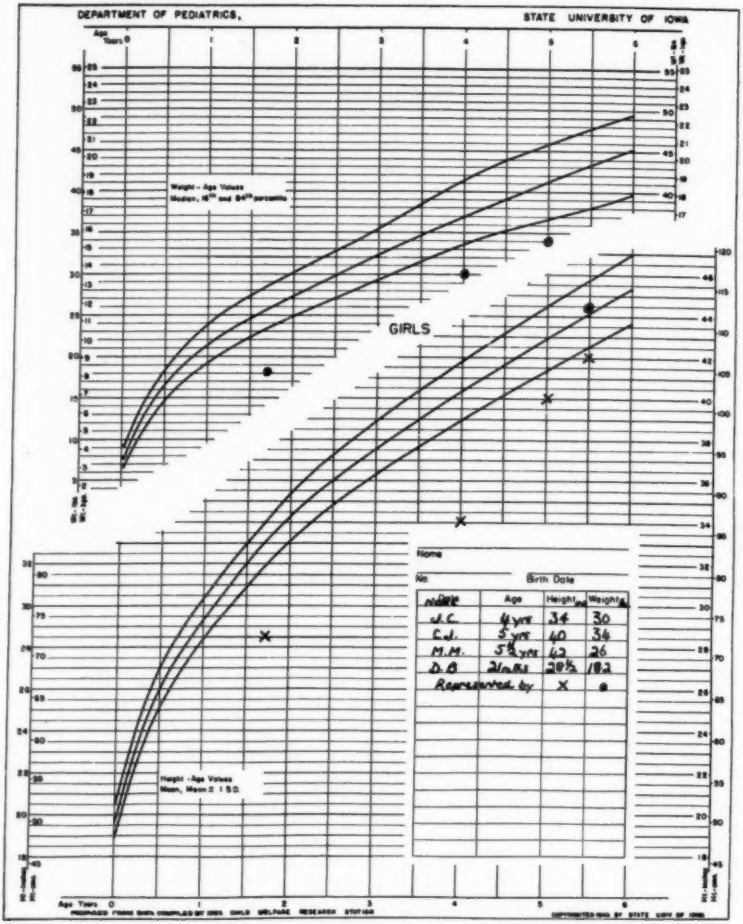

Fig. 42. Height and weight of girls on low phenylalanine diet.

TABLE 22. *Effect of Low Phenylalanine Diet upon Phenylketonuric Children*

AGE STARTED	I.Q. LEVEL				
	100 or Above (Normal)	90–99	70–89	50–69	30–49	1–29 (Low)
Up to 6 months	4	1	1	2	1	
7–12 months			1	1	1	1
13–18 months	1			3	1	2
19–24 months					2	2
25–36 months		1		1	1	6
37–48 months						3
49–60 months				3		4
61–72 months					1	

in the school years. Thus a child with a Cattell I.Q. of 120 at age 2 is just as likely to be slow as bright when he is a school age lad of 9. Clinical evidence suggests that predictions may be made about the future status of severely retarded children, but the extent of predictability has not been demonstrated as yet. Finally, there are isolated cases of untreated phenylketonurics whose mental development is not severely retarded.

WILSON'S DISEASE (HEPATOLENTICULAR DEGENERATION)

The condition of hepatolenticular degeneration was first described by Kinnier Wilson in 1912.[53] The condition is now considered to be due to an abnormality of copper metabolism resulting from a deficiency of the plasma protein ceruloplasmin.

Clinical Features

Convulsions sometimes herald the onset of the first symptoms of this disease, but these are not usually manifest until 10 to 15 years. Bulbar symptoms are usually first to appear. There is difficulty in articulation, hoarseness of the voice, and dysphagia. These conditions progress until there is a total loss of speech and inability to swallow. Patients gradually develop a parkinsonian facies, and there is often loss of emotional control with an exaggeration of weeping and laughter. Muscular rigidity appears, and the cog-wheel phenomenon is usually present. Kayser-Fleischer rings of brown or grayish pigment in the corneas of these patients can be seen, and cirrhosis of the liver occurs, but seldom gives rise to any symptoms. The intelligence of these patients is difficult to assess during the later stages of the condition because of inability of the patients to express themselves. Death ensues within a few years after physical deterioration has become extreme.

Inheritance

The condition is hereditary and is transmitted by an autosomal recessive gene. There is a high incidence of consanguinity among the parents of these patients.

Pathologic Findings

Postmortem investigations in Wilson's disease reveal widespread changes in the central nervous system, together with cirrhosis of the liver and rings of pericorneal pigmentation producing the Kayser-Fleischer rings. The brain damage consists in widespread degeneration. There is usually maximal degeneration, often cavitation of the lenticular nucleus, and there may be some degenerative changes in the cerebellum and cerebral cortex. Astrocytes showing large pale nuclei and irregular outlines known as Alzheimer's giant cells have been described as more or less characteristic of the process. Deposits of copper in the kidneys give rise to abnormalities of renal tubular function, and glycosuria, amino-aciduria and phosphaturia occur.

Pathogenesis

Patients with Wilson's disease are in positive copper balance. The lesion is now believed to be a deficiency of ceruloplasmin, a blue copper-containing protein in the serum.

Plasma copper occurs in two forms: (1) direct-reacting fraction bound to albumin, (2) indirect-reacting fraction corresponding to ceruloplasmin. In Wilson's disease experiments using injection of radioactive copper (Cu^{64}) can be used to demonstrate an alteration in copper-combining power in the serum. In the normal person an intravenous injection of Cu^{64} results in a rapid fall in serum radioactivity followed by a large increase some time later. In patients with Wilson's disease there is a slight fall initially and no secondary rise; since the secondary rise is due to Cu^{64} being incorporated into the ceruloplasmin, the failure to rise indicates a deficiency in that protein. This reaction has also been demonstrated with immunologic techniques by Scheinberg and Gitlin.[42]

Ceruloplasmin deficiency results in a decrease of the indirect-reacting fraction of copper. This causes (1) an increase of absorption of copper through the gastrointestinal tract, (2) an increase of direct-reacting copper in the plasma. Excess copper is then deposited in the tissues. Some of this surplus copper is then chelated with amino acid and excreted in the urine. This explains the increased absorption and excretion of copper among patients with Wilson's disease. Deposition of copper

in the various organs causes (1) lenticular degeneration of the brain, (2) cirrhosis of the liver, (3) Kayser-Fleischer rings in the cornea.

The relatively late onset of clinical symptoms in Wilson's disease is in part due to the gradual increase in the amount of copper in the tissues over a period of years.

Treatment

Without treatment Wilson's disease is invariably fatal. As present, treatment consists in repeated courses of BAL. Denny-Brown[12] suggests that 2.0 mg. per kilogram should be given intramuscularly twice daily for 10 days and the course repeated every 6 weeks to 6 months.

Penicillamine by mouth has been shown to increase the excretion of copper. A recent study by Walshe[50] indicates that the drug in dosages of 900 mg. daily is of value in treatment. Of the 22 patients treated, 3 showed no response, 11 showed limited improvement, and 6 became symptom-free. The remaining two received treatment with penicillamine before clinical evidence of neurologic involvement appeared. This showed a slower but in general better therapeutic effect by penicillamine compared with BAL. All cases showed cupruretic response, but there seemed to be no relation between the clinical and the biochemical response to the drug. In two cases the Kayser-Fleischer rings began to fade.

MAPLE SUGAR URINE DISEASE

In 1954 Menkes, Hurst and Craig[36] described a fatal condition characterized by cerebral symptoms and the passage of urine with an odor similar to that of maple sugar. This condition was originally described in the siblings of a family of six in whom the parents appeared unaffected. All four children died. They began to show clinical symptoms between the third and fourth days of life. There was difficulty in feeding, absence of the Moro reflex and development of irregular jerky respirations. This was followed by signs of spasticity and opisthotonos. The infants died within a few months. No treatment has been of any avail to these patients. The outcome has always been fatal.

The studies of Westall and his co-workers, of Mackenzie and Woolf and of Menkes indicate that the three branched amino acids, valine, leucine and isoleucine, are greatly increased in the urine, blood and cerebrospinal fluid of these patients. Indolelactic and indoleacetic acid are also excreted in excess amounts in the urine. They have also demonstrated the presence of large amounts of alpha-keto-isocaproic acid[52] and the keto analogues of leucine[11] together with lesser quantities of the keto acids of valine and isoleucine.[33] These findings would suggest that there is an impairment of the degenerative metabolism of the

branched chain amino acids[35] and that this may be important as the cause of the cerebral degeneration in this condition.

HARTNUP'S DISEASE

In 1956 Baron and his co-workers[4] described a clinical syndrome characterized by pellagra-like skin rash, neurologic changes, a consistent amino-aciduria and other biochemical changes suggesting a disturbance of nicotinic acid utilization. They named the condition Hartnup's disease after the affected family.

The first patient described with Hartnup's disease showed skin changes similar to those in pellagra. There was a rash over the exposed surfaces of the face, neck and hands which became more pronounced and began to ooze after being exposed to sunlight.

Neurologically, the patient presented a variable picture. At times he had only a mild ataxia. On other occasions he showed a coarse nystagmus, ptosis, an increase in deep tendon reflexes and poor performance of fine movements. There was a tremor of the outstretched hands and some spontaneous involuntary movements of his hands and tongue. In the later stages of the disease he became irritable. Psychological tests indicated that the patient was mentally retarded and that retardation was increasing.

The most consistent laboratory finding in patients with Hartnup's disease is a gross generalized amino-aciduria. This is renal in origin, since the plasma alpha-amino nitrogen levels are within normal limits. Milne and his co-workers[37] have shown that when tryptophan is administered to these patients, only 0.5 to 1.5 per cent of the ingested load appeared as kynurenine in these patients as compared with 3.07 to 7.0 per cent in normals. Furthermore, the pattern of excretion of indolic acids after tryptophan ingestion was grossly abnormal. Normally there is a sharp rise followed by a fall to normal levels within 8 to 10 hours. Indolelactic acid is the main indole derivative excreted after the ingestion of l-tryptophan and indole-3-lactic acid and after dl-tryptophan. In Hartnup's disease the high excretion persists for over 24 hours after ingestion of tryptophan. Indoleacetic acid was in greater amounts than indolelactic acid, and since lesser amounts of indolic acid were excreted after the dl- than the l-amino acid, they concluded that there is a defect in the transportation of both l- and d-tryptophan in Hartnup's disease. This defect affects not only the proximal renal tubules, but also the jejunum and possibly also the liver cells.

LEUCINE SENSITIVITY

In 1956 Cochrane and his co-workers[7] described 3 members of one family who had hypoglycemia with pallor, sweating and convulsions

after a large meal. Investigations showed the electroencephalogram to be within normal limits. Glucose, insulin and epinephrine tolerance tests were normal, and administration of ACTH and cortisone failed substantially to alter the blood sugar levels. Administration of casein, leucine and isovaleric acid, however, caused a fall of blood sugar to half the fasting levels within 30 to 45 minutes. The cause of the condition is not quite clear. Cochrane suggests two alternative mechanisms: (1) an increased effect of circulating insulin on intracellular carbohydrate metabolism, (2) an increased secretion of insulin by the islets of Langerhans.

These patients have relatively little trouble so long as high protein meals are avoided. Hypoglycemia due to leucine sensitivity may be identified by feeding a test dose of casein (1.5 gm. per kilogram) and leucine (0.15 gm. per kilogram) to the fasting subject and noting the blood sugar levels at frequent intervals during the next 90 minutes.

ARGININOSUCCINIC ACIDURIA

This condition was first described by Allan and his co-workers[1] in 1958. Two siblings were described showing severe mental retardation. Both children had grossly abnormal electroencephalograms, and one had severe epileptic attacks followed by ataxia lasting several days. Both children had friable hair and a systolic murmur in the heart, but otherwise differed little from other retarded children. Westall[51] isolated the abnormal compound and found that it was l-argininosuccinic acid, a well known intermediate in the urea cycle. The substance is present in the cerebrospinal fluid in a concentration two to three times greater than in plasma. It is not certain whether the condition is simply a metabolic block due to deficiency of an enzyme for which argininosuccinic acid is a substrate or whether it is a more complicated disorder.

CYSTATHIONINURIA

In 1958 Harris[18] described an elderly imbecile who excreted about 500 mg. of cystathionine. Excretion was consistent, and there was little or no reabsorption. When the patient died, there appeared to be greater amounts of cystathionine in extracts of liver and kidney than in controls, so that the accumulation appeared to be an "overflow" type and not renal in origin. Since the brother and a nephew of the patient excreted moderate amounts of cystathionine, the condition could be hereditary and represent a genetically determined defect of enzyme formation. Cystathionine is an intermediary in the conversion of methionine to homoserine and cystine. Excess feeding of methionine in this patient led to an increase in the rate of excretion of cystathionine.

This suggests that there was a deficiency in the enzyme system which normally cleaves cystathionine into cystine and homoserine.

DISORDERS OF CARBOHYDRATE METABOLISM

GALACTOSEMIA

About 50 years ago the German physician von Reuss[41] reported a case of an 8-month-old infant with marasmus and melituria. The melituria disappeared when milk was eliminated from the diet, but the infant died before further tests could be done. Subsequently other such cases were found.[17, 34, 39] In each instance the infant appears normal at birth, but after a few days of milk feeding he starts to vomit, becomes lethargic, and fails to gain weight, and enlargement of the liver becomes apparent. Ascites and edema may develop, and if the condition is severe, death occurs, owing to malnutrition and wasting. Infants who survive are usually malnourished, and dwarfed at two to three months of age, and mental retardation and cataracts may be discerned. In others cirrhosis of the liver develops months or years after the acute phase of the disease. In all instances the signs and symptoms regress after deletion of milk and milk products from the diet.

Pathogenesis

Although it has been known for many years that galactosemia represents a congenital defect of the liver in which the conversion of galactose to glycogen is in some way damaged, it was not until the early 1940's that a series of brilliant studies by LeLoir and his coworkers[31] in Argentina demonstrated the pathway by which galactose was converted to glucose, as shown in Figure 43. It was found that galactose was converted to glucose-1-phosphate by means of four separate steps, each of which was catalyzed by a specific enzyme.

In 1955 Schwarz et al.[44] in Manchester, England, showed that when milk was given to a galactosemic child, there was an abnormal accumu-

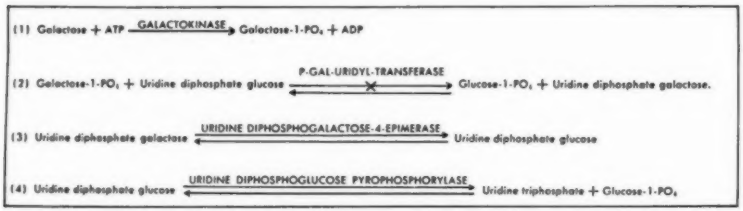
(1) Galactose + ATP —GALACTOKINASE→ Galactose-1-PO4 + ADP
(2) Galactose-1-PO4 + Uridine diphosphate glucose ⇄ (P-GAL-URIDYL-TRANSFERASE) Glucose-1-PO4 + Uridine diphosphate galactose.
(3) Uridine diphosphate galactose ⇄ (URIDINE DIPHOSPHOGALACTOSE-4-EPIMERASE) Uridine diphosphate glucose
(4) Uridine diphosphate glucose ⇄ (URIDINE DIPHOSPHOGLUCOSE PYROPHOSPHORYLASE) Uridine triphosphate + Glucose-1-PO4

Fig. 43. Pathway of galactose metabolism.

lation of galactose-l-phosphate in the red cells, though this metabolite was not present in normal children. This meant that the block must occur somewhere beyond galactose-l-phosphate, or that galactokinase, the enzyme needed for the first reaction, was present in adequate amounts. In 1956 Kalckar and his co-workers[29] in the United States demonstrated that uridine diphosphogalactose-4-epimerase and uridine diphosphoglucose pyrophosphorylase, the enzymes needed for the third

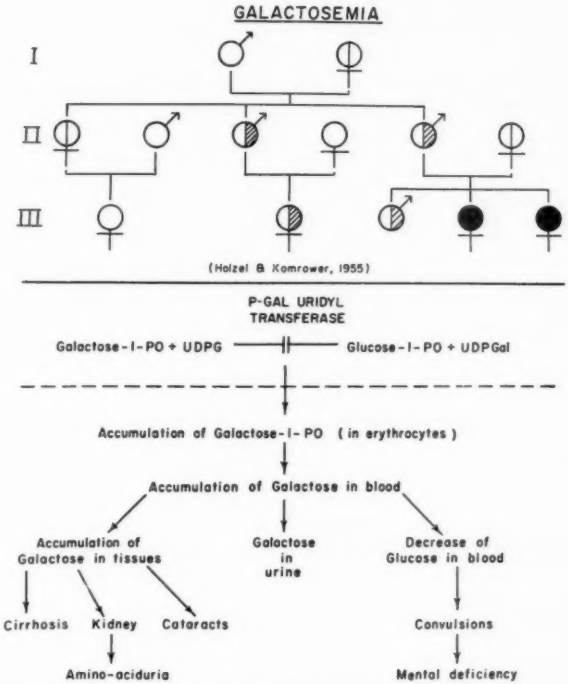

Fig. 44. Pathogenesis of galactosemia. (After D.Y.-Y. Hsia: *Inborn Errors of Metabolism*. Year Book Publishers, Inc.)

and fourth steps, were present in normal amounts in the erythrocytes of galactosemic children. Nevertheless, galactose-l-phosphate uridyl transferase, the enzyme needed for the second step, was barely detectable in 10 such children. From this they concluded that galactosemia occurs as a result of an enzyme deficiency which causes a metabolic block in step (2) and that all the other properties of metabolism in such patients were normal and intact.

Decrease or absence of galactose-l-phosphate uridyl transferase results in accumulation of galactose-l-phosphate in the red cells, and this

in turn is responsible for accumulation of galactose in the blood. The excessive galactose can have three kinds of effects (Fig. 44): (1) Galactose and galactose-l-phosphate can accumulate in the tissues and over a period of time are probably responsible for cirrhosis of the liver, cataracts, and renal changes which are also responsible for amino-aciduria. (2) Galactose can be excreted in the urine, and (3) galactose depresses the blood glucose level, and this in turn causes convulsions and mental retardation.

Inheritance

Galactosemia is transmitted by an autosomal recessive gene. The defect has been noted among siblings in about half of the families reported, and it would be expected to occur in one out of four births in such families with a normal distribution.

The heterozygous carrier of the abnormal gene may be detected by a decrease of galactose-l-phosphate uridyl transferase among parents of such children. By using the oxygen uptake method it has been shown that the parents have levels approximately half that seen in normal controls.[23]

Diagnosis

Galactosemia can be diagnosed by three different means:

1. Galactose in the Urine: Galactose in the urine may be identified in the following ways:

Mucic Acid Test. Urine, 50 ml., and concentrated nitric acid, 12 ml., are heated in a water bath and cooled overnight. A fine white precipitate of mucic acid will form if lactose or galactose is present. These crystals can be identified under the microscope and by their melting point (217 to 218° C.).

Osazone Test. Clarified and concentrated urine, 25 ml., is mixed with phenylhydrazine, hydrochloride and sodium acetate and heated in a water bath for 45 minutes. The crystals that appear can be compared with the osazone prepared from pure galactose. After 3 recrystallizations the crystals should melt constantly at 182° C., and when mixed with a known specimen containing galactosazone, there should be no depression of the melting point. The osazone can also be compared with that prepared from galactose by paper chromatography.

Paper Chromatography. Galactose can be identified in the urine by using one-dimensional chromatograms with butanol-ethanol-ammonia as solvent and aniline phthalate as developer and comparing the unknown with known galactose standards.

2. Galactose Tolerance Tests. Galactose tolerance can be determined by two different means: the oral and intravenous.

1. For the *oral group galactose tolerance test* 1.75 gm. per kilogram of body weight of galactose is given by mouth on a fasting stomach. Duplicate 0.2-ml. capillary blood samples are collected before feeding and at 30, 60, 90, 120 and 240 minutes after feeding.

2. *Galactose-1-Phosphate Uridyl Transferase Activity.* This is performed by the method described by Anderson, Kalckar, Kurahashi and Isselbacher.

REAGENTS.* 0.9 per cent sodium chloride uridine diphosphoglucose (UDPG) 5μm. per ml., galactose-1-phosphate 7.5 μm. per ml. (barium-free), tris glycine buffer 0.2 ml., pH 8.1, UDPG dehydrogenase 800 units per ml.

PROCEDURE. Approximately 5 ml. of blood are collected in heparinized tubes. The red cells are washed twice with a double volume of 0.9 per cent sodium chloride and hemolyzed by the addition of an equal volume of cold distilled water. The hemolysate (0.25 ml.) is then incubated with UDPG, galactose-1-PO_4, and tris glycine buffer for 30 minutes at 37° C. For each sample a control is run wherein no galactose-1-PO_4 is added to the substrate. After incubation UDPG is determined in heat-inactivated hemolysates by means of UDPG dehydrogenase. The difference between the measurements of UDPG in the sample and control represents the amount of UDPG consumed through the activity of Gal-1-P-uridyl transferase. Uridine diphosphoglucose pyrophosphorylase activity is also determined to assure that the blood sample and the hemolysate are properly handled.

INTERPRETATION. The means of Gal-1-P-uridyl transferase activity were found to be 4.5 (± 0.47) gm. of hemoglobin for normal and 0.5 (± 0.04) for galactosemic patients.

Treatment

The principle of all treatment centers around the use of lactose and galactose-free diets. During early infancy preparation of a galactose-free diet requires considerable ingenuity, though prescriptions for such diets are available. Proprietary preparations such as Nutramigen (manufactured by Mead Johnson & Company) and Mulsoy (manufactured by Borden Company) are more convenient. These contain up to 1 per cent of galactose, but in this concentration galactose is probably not harmful to galactosemic patients.

When the patient becomes old enough to take semisolid or solid foods, dietary prescription is relatively simple. All unprocessed fish and animal products may be regarded as galactose-free with the exception of "brains." Fresh vegetables, except peas, and fresh fruit are permissible. Creamed cheeses generally contain lactose, but cheddar cheeses do not. There are many canned preparations of vegetables, meats and cereals suitable for infant feeding which contain no milk, but caution is necessary when using processed foods, since some of these may contain milk powder. In general, those containing whey, buttermilk solids and nonfat dry milk should be avoided. The galactose content is low but variable, and it may be necessary to obtain concentrations from the manufacturer. Most kinds of breads and rolls contain milk, but bread made from cracked wheat and "Vienna bread" are useful exceptions. Supplements of calcium are advisable for infants and children, since their dietary sources of the mineral have been eliminated.

RESULTS. We have had the opportunity to observe 14 patients with galactosemia in our clinic. The results are summarized in Table 23. The enzyme assays were performed by both the UDPG consumption method[2] and the manometric method.[23] Intelligence was assessed by

* All reagents may be obtained from Sigma Chemical Co., St. Louis 18, Missouri.

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TABLE 23. *Summary of Clinical Findings in 14 Cases of Galactosemia*

		CLINICAL FEATURES			GALACTOSE-FREE DIET		INTELLIGENCE		ERYTHROCYTE		
Patient	Date of Birth	Manifestations	Time of Onset	Age at Diagnosis	Age at Introduction	Nature of Diet	I.Q. Score	Age When Tested	P-Gal Transferase Activity 1.	2.	Comment
CK ♀	11/5/1946	Diarrhea, wasting, hepatomegaly	Soon after birth	4 months	4 months	Strict	109	12½ yrs.	1.3	8.9	
AK ♂	11/13/1950	Jaundice, hepatomegaly	Soon after birth	7th day	7th day	Occasional ice cream, milk shake	110	8½ yrs.	0	8.7	Brother of CK
TJ ♂	12/28/1948	Vomiting, cataract, headaches, shivering, fainting	Soon after birth Early childhood	9 yrs. 2 months	9 yrs. 2 months	Strict	121	10 yrs. 2 months	0.6	6.7	Milk intake restricted from infancy. Probably had hypoglycemic attacks
SJ ♀	3/11/1953	Vomiting Chills, headaches, cataracts	Soon after birth Early childhood	5 years	5 years	Strict	116	6 years	1.0	8.7	Milk intake restricted from late infancy. Sister of TJ
JM ♂	5/4/1948	Jaundice, cataracts, edema	Soon after birth	4 months	4 months	Had some milk products	119	10 yrs. 11 months	0.7	0.4	
RM ♂	4/2/1954	Jaundice, cataracts	Soon after birth	1 month	1 month	Had some milk products	110	5 years	0.3	7.8	Brother of JM
DP[1] ♂	11/27/1949	Vomiting, diarrhea, poor weight gain, jaundice	Soon after birth	22 months	1st week of life	Probably strict	102	9 yrs. 4 months	0.1	6.7	Nutramigen given empirically after birth
DP[2] ♂	8/16/1951	Jaundice, vomiting, diarrhea, poor weight gain	Soon after birth	10th day	10th day	Strict	81	7 yrs. 7 months	0.3	4.2	Brother of DP[1]

MM ♂	7/2/1951	Reluctance to feed, loss of weight, hepatomegaly, cataracts, convulsions	Soon after birth Early childhood	1 month	1 month	Not certainly known	48	7 yrs. 9 months	0	—	Has dysphasia
CP ♀	2/27/1953	Lethargy, jaundice, vomiting, cataracts, convulsions	Soon after birth	2½ yrs.	1½ yrs.	Strict	59	6 years	0	—	Refused milk since age 1½ years
BR ♀	7/25/1955	Jaundice, hepatomegaly, edema, cataracts	Soon after birth	6 weeks	8 weeks	Strict	95	3 yrs. 8 months	1.1	—	Sister of CP
GD ♂	3/16/1956	Jaundice, hepatomegaly	Soon after birth	1 month	1 month	Strict	97	3 years	0.8	8.6	
WS ♂	8/31/1958	Vomiting, diarrhea, jaundice, hepatomegaly, ocular hemorrhage	3rd day	1 month	1 month	Strict	100	1 year 4 months	0.3	2.5	V.A.—perception of light only
RW ♂	1894	Thought to have diabetes mellitus for past 11 years. Now has cirrhosis of liver, cataracts	Since childhood	62 years	62 years	Avoids milk	Normal		0.9	8.0	Grandfather of TJ and SJ. I.W. not estimated, but has held responsible business position

Initial diagnosis made on galactosemia: typical symptoms, response to diet, and usually also abnormal galactose tolerance test.
Strict diet: no milk or food known to contain milk. Milk substitute used.
Enzyme Determinations (Gal-1-PO_4 uridyl transferase):
Method: 1. UDPG consumption test.[9]
2. Manometric method.[25]
Intelligence testing:
All assessments made by one observer.
All except WS tested on Revised Stanford-Binet Scale (Form L).
WS Maxfield Buchholz modification of Vineland Social Maturity Scale for Blind Children.

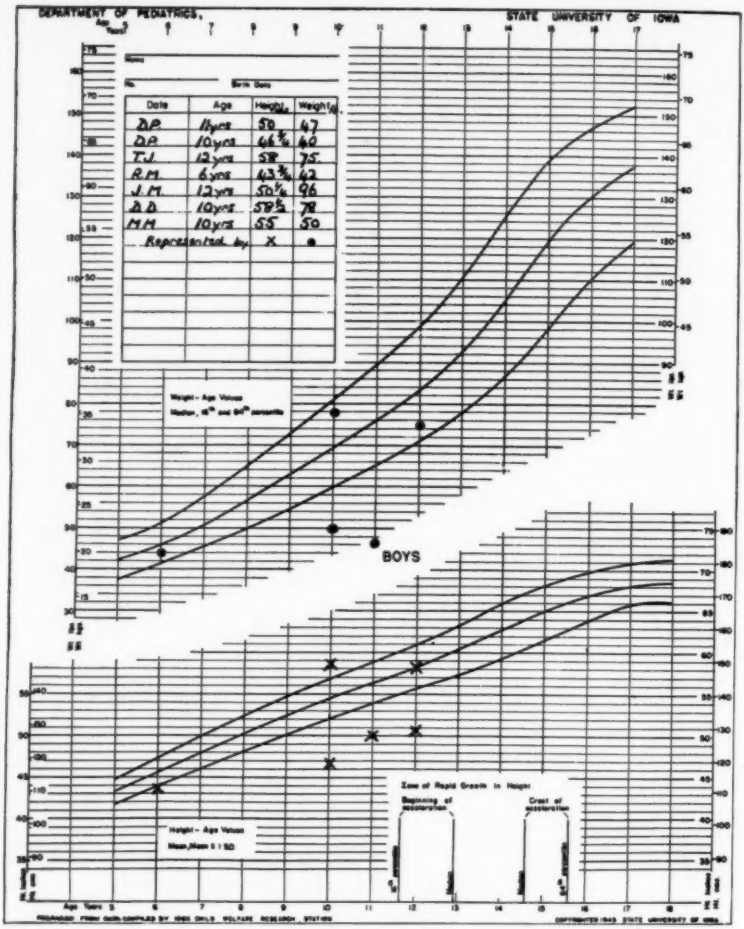

Fig. 45. Height and weight of boys on lactose-free diet.

the 1937 Revision of the Stanford-Binet Scale, Form L, in all cases except that of V.S., for whom the Maxfield Buchholz modification for blind children of the Vineland Social Maturity Scale was used.

Twelve of the 14 patients are lively and healthy, but thin (Figs. 45, 46). No recent follow-up is possible in the case of N.N.; R.W. has cirrhosis of the liver. An important and disappointing result of treatment lies in the fact that 8 of the 14 have had visual difficulty (due to cataracts, and bilateral intraocular hemorrhages in one), resulting in various blocks in visual activity. Cataract formation has been re-

ported in galactosemia by the fourth day of life with suggestion that mothers of galactosemic children, the heterozygotes of galactosemia, may not be able to metabolize the increased amounts of galactose found in the blood during pregnancy. Transplacentral pathway of galactose-l-phosphate could result in damage to the fetal lens. Four of our patients, in spite of treatment by four months of age, have residual visual difficulty, and assuming that their dietary treatment was lactose and galactose-free, it is difficult to suggest means of avoiding these complications.

In nine of the 14 patients the diagnosis of galactosemia was made

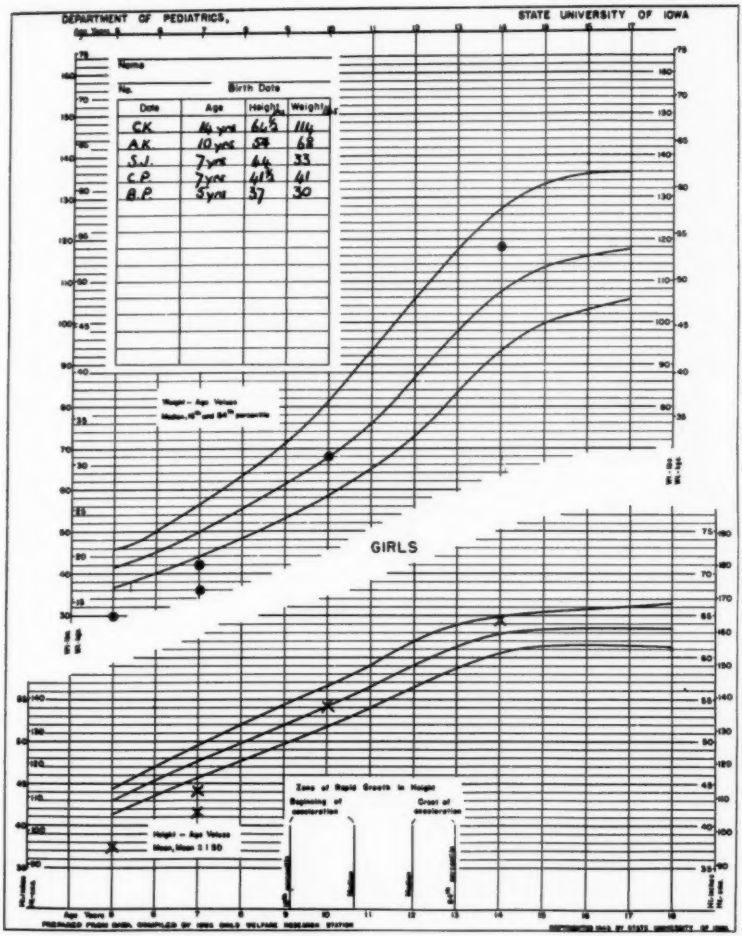

Fig. 46. Height and weight of girls on lactose-free diet

TABLE 24. *Effect of Lactose-Free Diet upon Intelligence in 46 Cases of Galactosemia*

	INTELLIGENCE		
	Normal	Moderate Retardation	Severe Retardation
Adequate dietary control:			
Males	9	3	2
Females	6	1	0
Total	15	4	2
Inadequate dietary control:			
Males	5	5	7
Females	2	5	1
Total	7	10	8

Based upon reported cases and upon reports from the Genetic Clinic.

by 4 months of age. Of these, eight have normal intelligence, and the ninth (M.M.) is considerably retarded. Contact with the latter patient has been poor, and it is likely that for economic and other reasons the diet did not remain galactose-free. In five of the 14 patients medically supervised diet was not started until at least 22 months of age. Of these, one shows mental retardation (C.P.). Of the four with normal intelligence, two (C.J. and S.J.) had had restrictive milk intake from late infancy because milk ingestion was observed to produce vomiting and other symptoms, and another (D.P.) received Nutramigen shortly after birth because of consistent diarrhea and vomiting. The fourth member is interesting because, although he remained undiagnosed and untreated for 62 years, he has led a successful life as a business executive.[24]

These cases, together with others published in the literature, are summarized in Table 24. These show that, as in phenylketonuria, adequate dietary control in the early months of life is a factor in the height of intelligence finally obtained. Exceptions do occur, however, and the outcome cannot always be predicted for certainty despite optimal clinical management. Also, it would appear that a greater proportion of untreated patients with galactosemia escape mental deficiency. This may of course be due to the development of the UDPG galactose pyrophosphorylase, which can serve as an accessory pathway to galactose metabolism as the child gets older.[26]

GLYCOGEN STORAGE DISEASE

"Glycogen storage disease" is an over-all term applied to a group of congenital and familial disorders characterized by deposition of abnormally large quantities of glycogen in the tissues. At least two of the six or seven types of the disease are of neurologic importance.

In 1953 Forbes[15] described a number of cases of glycogen storage

disease of skeletal muscle clinically resembling Werdnig-Hoffmann disease. These patients had progressive weakness, difficulty in swallowing, and regurgitation of food. Also, there was macroglossia, cardiomegaly and hepatomegaly. Laboratory studies showed a normal response to glucose tolerance tests and to epinephrine. Histochemically, however, the muscles were found to be loaded with glycogen. Autoglycogenesis occurred to a degree, but less than in normal tissues. Studies of the molecular structure of the glycogen in muscle showed an excessive number of branched linkages with a chain length shorter than average, suggesting that there is a deficiency of the debrancher enzyme, *amylo-1,6-glucosidase*.[8]

In 1941 McArdle[32] described a muscle disorder characterized by rapid exhaustion of otherwise mechanically and physiologically normal muscle. This could be prevented by intravenous administration of lactate, glucose or fructose. He suggested that this may result from a metabolic block in the ability to convert glycogen to lactic acid and described the condition as a "myopathy due to a defect in muscle glycogen breakdown." This condition has recently been restudied,[19, 38] and muscle from these patients has been found to have considerable amounts of glycogen with normal structure. Detailed studies showed that most of the enzymes involved in glycolysis were normal. However, *phosphorylase* was notably deficient.

DISORDERS OF LIPID METABOLISM

GAUCHER'S DISEASE (INFANTILE FORM)

This is a lipid storage disease of the reticuloendothelial system characterized by the presence of large pale cells in the affected tissue. Infants affected with acute Gaucher's disease are usually normal at birth, but at the fourth month they begin to exhibit apathy together with progressive physical and developmental retardation. The abdomen becomes enlarged, first the spleen and then the liver increasing in size. As the condition progresses the child's movements become slow. The eyes fail to fix upon objects, although sight remains intact. Muscular rigidity develops with some increase in the tendon jerks, and opisthotonos gradually develops. Dysphagia, choking spells with severe cough and intermittent cyanosis are caused by increasing pulmonary involvement. Death usually occurs during the first year to 16 months of life.

The clinical entity characterized by the presence of Gaucher cells may represent at least three genetically distinct groups. In a few families the condition is transmitted by an autosomal dominant gene; in the majority it is caused by an autosomal recessive gene; and in the third group there is always neurologic involvement in addition to the

usual changes in the bone, liver and spleen, and the condition also appears to be transmitted by an autosomal recessive gene.[22] At present it is not known whether these genes represent a system of separate alleles at one locus, or are located at separate loci.

Pathogenesis

Laboratory studies show that in Gaucher's disease the serum lipid and cholesterol levels are normal. No alteration in fat absorption has been found, and no change in serum cerebrosides has been demonstrated. However, three substances have been isolated in abnormal quantities from tissues containing Gaucher cells: (1) a galactosiderocerebroside (kerasin), (2) a glucosiderocerebroside, (3) a water-soluble glycolipid called polycerebroside.

Some workers suggested that the condition represents a disturbance of intermediate lipid metabolism, leading to an accumulation of cerebrosides in the serum and secondarily to storage of the abnormal substance in the reticulum cells. Thannhauser,[47] however, feels that the primary disfunction is an enzyme disturbance in the reticulum cells causing an increased synthesis of cerebrosides which leads to rapid storage of these substances within the cell.

Uzman[48] has shown that there is much less of the water-soluble glycolipid in the spleens of older patients with Gaucher's disease than in those of younger patients, though histologically both show heavy engorgement with Gaucher cells. He wonders whether this compound represents a transitional stage which finally results in kerasin formation, since in Tay-Sachs disease there is a great abundance of gangliosides in the central nervous system. Since there is great similarity between gangliosides and polycerebrosides, this may help to explain the neurologic changes in infantile Gaucher's disease.

The diagnosis is established by aspiration of bone marrow. There is the characteristic accumulation of pale, poorly staining material in the large cells, often multinucleated with "wrinkled" cytoplasm.

NIEMANN-PICK DISEASE

This condition has many clinical features in common with Gaucher's disease, but appears to be more diffusely spread. The condition presents a variable neurologic picture. Affected infants appear normal at birth, but soon exhibit both physical and mental retardation. There is wasting of the extremities and protuberance of the abdomen as both liver and spleen enlarge. A cherry-red spot is present in the macula in somewhat less than half the patients. The infants remain dull and apathetic mentally and usually die between the ages of six months and

five years from anemia and emaciation. In recent years a few cases of an adult or chronic type of the condition have been described. The patients have characteristic Niemann-Pick cells in the liver, lungs and lymph nodes, but show none of the clinical signs and symptoms described above.

This condition is transmitted by an autosomal recessive gene which seems widely distributed throughout the world. The heterozygous carrier is not detectable.

The characteristic cells are large and pale with foamy vacuolated cytoplasm. The liver, spleen, lung and lymph nodes are primarily involved, but degenerative changes in the ganglion cells are found in the central nervous system, and the cherry-red spot at the macula has been observed in rather less than half the cases described.

The cellular deposit appears to be a sphingomyelin accumulation. Thannhauser has suggested that in this disease the mechanism for conversion of ceramide to sphinogomyelin is intact, but that the reverse process fails to occur normally.

AMAUROTIC FAMILY IDIOCY

Amaurotic family idiocy is an over-all term applied to several distinct but probably related disturbances in lipid metabolism. These may be divided clinically into (1) infantile form, Tay-Sachs disease; (2) late infantile form, Bielschowsky-Jansky disease; (3) juvenile form, Spielmeyer-Vogt disease; (4) late juvenile form, Kufs disease.

Tay-Sachs Disease

Tay-Sachs disease is a familial disease characterized by progressive mental deterioration with the presence of a cherry-red spot in the macula. Children affected with Tay-Sachs disease appear to be essentially normal up to four to six months of age, when they become irritable, especially to sound, and the rate of development becomes slower and muscle power weaker. Eye changes are heralded by failure to fix the eyes and to recognize the mother. Sight seems to fail gradually, and blindness ensues. Irritability increases, and there are occasional bursts of explosive laughter. Early in the disease muscular spasticity and hyperflexion occur. There are muscular twitchings and convulsions. Mental deterioration gradually produces idiocy, and the condition usually terminates in a state of decerebrate rigidity and respiratory infection.

The condition is transmitted by a rare recessive gene and has been found to be prevalent among people of Hebrew ancestry. About 10 per cent of the patients are not Jewish, however, and the incidence of consanguinity among these patients is noticeably higher.

Histologically, the brain shows widespread changes in the ganglion cells. The cells swell, and the nuclei become displaced to the periphery and eventually disintegrate. Staining shows that the swelling is due to large droplets of lipoid material. Demyelinization occurs secondarily to the destruction of the ganglion cells, and the microglia become ameboid and distended with the debris of the cellular disintegration. The process in the retina is identical with that in the brain. The ganglion cells swell with lipids, causing the white appearance. The macula remains transparent, and the choroidal blood vessels remain visible as a cherry-red spot which is accentuated by the white surroundings.

The pathogenesis of Tay-Sachs disease is completely unknown. The blood lipids do not seem to be disturbed, but there is excessive lipid deposition in the ganglion cells throughout the brain and central nervous system, and this is followed by degeneration. Excessive lipid deposits in the ganglion cells of the retina cause the whitish appearance of the retina and accentuate the cherry-red spot at the macula.

Bielschowsky-Jansky Disease

This differs from Tay-Sachs disease in that the age at onset is between three and four years and the condition runs a somewhat slower course. The cherry-red spot at the macula is not found, but there is optic atrophy and some pigmentation of the retina.

Spielmeyer-Vogt Disease

The age at onset of this condition is between five and six years. The condition runs a slower course than Tay-Sachs disease, and death usually occurs by about 15 years. The cherry-red spot is usually present in this form of the disease, but is less well defined, and pigmentation of the retina is often seen. Unlike Tay-Sachs disease, this condition is not found predominantly among Jewish families, and the lipoid deposits have been characterized as having a higher melting point of 195° C. and containing nitrogen and sugar. In this respect the disease seems similar to the lipoidoses of Gaucher and Niemann-Pick. It would seem, therefore, that the condition is genetically distinct from Tay-Sachs disease, though clinically similar.

Kufs Disease

The age at onset of this condition is between 15 and 25 years. The condition differs from Tay-Sachs disease in that there is usually no loss

of vision. Retinitis pigmentosa has been described among relatives of these patients.

GARGOYLISM (HURLER SYNDROME)

This condition is characterized by grotesque features associated with mental retardation, cardiac murmurs, corneal opacities and sometimes deafness. The skeletal defects were first described by Hurler[25] in 1917 and the mental retardation and corneal opacities two years later.

The general appearance of patients with gargoylism is grotesque. The patients are small in stature with short necks and dorsolumbar kyphosis. The head is enlarged and scaphocephalic, the lips are coarse, eyes set wide apart, and the ears are low. The skin is dry and the hair coarse. There is a diffuse clouding of the cornea, and often deafness. The abdomen is protuberant with a hepatosplenomegaly, and hernias are frequently present. There is some limitation of joint movement. X-ray films show widening of the skull sutures and enlargement of the anterior fontanel. The long bones, phalanges and ribs seem broader and shorter than normal, and there is sometimes delay in the appearance of centers of ossification. In the heart there is a fibrous thickening of the valves, and many patients die from cardiac failure. Mental retardation is noticed fairly early in these patients and is progressive, so that many gargoyles are institutionalized by the time they reach adult life. Occasionally convulsions occur.

Gargoylism is inherited by two distinct genetic mechanisms, and the two types are genetically distinct from each other.

1. Transmission by an autosomal recessive gene in which males and females are equally affected. Corneal clouding occurs in affected persons, but seldom deafness. This type accounts for about one third of the cases of gargoylism.

2. Transmission by a sex-linked recessive gene. Only males are affected. Corneal clouding is never seen, but about 43 per cent of these gargoyles are deaf.

There is no known way of detecting the heterozygous carrier in gargoylism.

The brain is reduced in weight in these patients, and dilatation of the ventricles is often found. The neurons are swollen and contain granular deposits. Fusiform swellings may be seen on the dendrites of Purkinje, and the white matter in the brain may be thin and shrunken. The cornea shows deposits in the middle and posterior layers. The liver is often enlarged with granular deposits to be seen within the cells. Similar deposits have also been found in the spleen, kidney, heart, intestine, pancreas, pituitary and aorta.

The deposits found in the cells seem to be of two types:

1. Brante[6] described one of them as a mucopolysaccharide similar to or identical with chondroitin sulfuric acid. A similar substance has been identified in the urine of patients with gargoylism.[13]

2. Uzman[49] identified the second storage substance in the tissues of gargoyles as a water-soluble glycolipid. He suggests that accumulation of the mucopolysaccharide is the primary metabolic defect and that the glycolipid appears as a result of the interference in cellular metabolism resulting from this accumulation.

MISCELLANEOUS METABOLIC DISORDERS

HEREDITARY PERIODIC PARALYSIS

This is a rare clinical entity characterized by intermittent attacks of flaccid paralysis of the muscles of the extremities and loss of the deep tendon reflexes.[46] The attacks are frequently preceded by a prodromal period when patients feel tired or irritable, or sometimes have a sense of apprehension for several hours before the actual attack. In the typical case paralysis begins peripherally in the legs and progresses centrally until the patient becomes completely helpless and unable to move. After a few hours the muscles begin to recover gradually, starting with the central muscles, which were the last to become affected, and followed by the more peripheral ones. Episodes of paralysis may occur as often as several times weekly, and are usually associated with a decrease in the concentration of potassium in the serum.

The condition appears to be transmitted as an autosomal dominant, and tends to affect males more frequently than females. In most instances symptoms appear about the time of puberty, few examples having been reported as beginning during early infancy or childhood.

Oral administration of 2 to 10 gm. of potassium chloride is effective in stopping an acute attack.

HYPERKALEMIC FAMILIAL PARALYSIS (ADYNAMIA EPISODICA HEREDITARIA)

Recently several instances of hereditary periodic paralysis associated with an increase of serum potassium have been reported.[16] The disease is clinically similar to familial periodic paralysis in that it is characterized by episodes of flaccid paralysis followed by spontaneous recovery and symptom-free periods. Unlike periodic paralysis, the serum potassium rises during attacks, and administration of potassium salts precipitates attacks instead of preventing them. The increase in concentration of potassium in plasma is thought to result from a shift of potassium from the intracellular to the extracellular spaces.

This condition appears to be transmitted by a single autosomal gene with almost complete penetrance.

CONGENITAL NONHEMOLYTIC JAUNDICE WITH KERNICTERUS

In 1952 Crigler and Najjar[9] reported on a group of infants from an isolated community in western Maryland who had an elevated indirect bilirubin level and increasing signs of extrapyramidal tract involvement. Infants with the condition exhibit jaundice early, often on the second day of life. There is an increase of indirect bilirubin fraction to levels between 25 and 45 mg. per 100 cc. The infants have spasticity, rigidity and opisthotonos and often die in the first year of life. At autopsy there is staining of the basal ganglia, but the liver shows no abnormality except the presence of bile thrombi in the hepatic canaliculi.

It is generally agreed that bilirubin is converted to "direct" bilirubin by the following reaction:

$$\text{Uridine diphosphate glucuronic acid (UDPGA)} + \text{bilirubin (indirect)} \xrightarrow{\text{liver}} \text{bilirubin glucuronide (direct)} + \text{uridine diphosphate (UDP)}$$

This reaction is catalyzed by an enzyme system in the microsomes of the mammalian liver which appears to be the same system that conjugates such substances as o-aminophenol or phenolphthalein with glucuronic acid.

Bilirubin from the serum of patients with congenital nonhemolytic jaundice with kernicterus has been crystallized by ammonium sulfate fractionation and found to be of unconjugated type. Also, bilirubinemia is absent, and the urine in these patients is colorless and contains only traces of unconjugated bilirubin. Finally, the glucuronide formation of menthol, of salicylate and of the metabolites of hydrocortisone is greatly depressed, which indicates that this condition represents a metabolic block at the stage of bilirubin conjugation and probably is due to a specific enzyme defect.[43] It is well known that infants with raised indirect bilirubin levels due to erythroblastosis fetalis and prematurity are liable to suffer kernicterus. It is thought that the patients who have jaundice due to a deficiency of the conjugating enzyme also suffer kernicterus by the same mechanism.

The condition appears to be transmitted by a single autosomal recessive gene. There is a high incidence of consanguinity among the cases described.

Exchange transfusion temporarily lowers the serum bilirubin levels and may be helpful during the first weeks of life when the brain is presumably most susceptible to damage.

DEFICIENCY OF PSEUDOCHOLINESTERASE

Suxamethonium (Succinyldicholine) is a chemical compound used by anesthetists to induce relaxation of muscles. The duration of its action is relatively short because it is soon destroyed by the pseudocholinesterase in the plasma. However, if the patient has a low pseudocholinesterase, a genetically determined defect, he is likely to have prolonged apnea following its use.

Kalow[30] has divided the population into three groups by measuring dibucaine numbers. A dibucaine number is a measure of the degree of inhibition of serum cholinesterase obtained with dibucaine under standard diet conditions and is expressed as a percentage.

1. Dibucaine numbers 71 to 85 are all obtained from normal persons.
2. Dibucaine numbers 58 to 66 are obtained from a group of people who are probably heterozygote carriers of the abnormality.
3. Dibucaine numbers 55 or less are obtained from persons who are sensitive to suxamethonium and are probably homozygotes for the trait.

Kalow and his co-workers suggest that the abnormal dibucaine numbers in suxamethonium-sensitive persons are a part of the typical pattern of substrate passivity and inhibition characteristics of serum cholinesterase which is present, and they suggest that this is due to the synthesis of an enzyme protein differing structurally in some way from that synthesized in some people.

FAMILIAL CRETINISM WITH GOITER

During the last decade a number of inborn errors of metabolism associated with a disturbance of thyroid metabolism have been described.[45] Characteristically the infant cretin appears normal at birth, but sluggish behavior may be noticed in the first six weeks of life. Thereafter the skin gradually becomes dry and coarse, the abdomen protuberant, the lips thick and the voice hoarse. The child is often constipated. In untreated cases the child has severe and irreversible mental retardation.

Three types of familial cretinism have been described. The biosynthesis of thyroid hormone takes place through a series of separate steps (Fig. 47). (1) Iodide and various forms of iodine enter the body through the intestinal tract and are distributed throughout the extracellular compartment of the body. (2) Some of the iodide is excreted through the kidneys, but most of it is trapped within the thyroid gland and oxidized to elemental, or free, iodine. The trapping process requires oxygen and is undoubtedly enzymatically controlled. A defect in this step results in *cretinism from a failure of organic iodine to form.* (3) The free iodine then reacts with tyrosyl residues to form monoiodotyrosine and diiodotyrosine. (4) Some of the iodinated

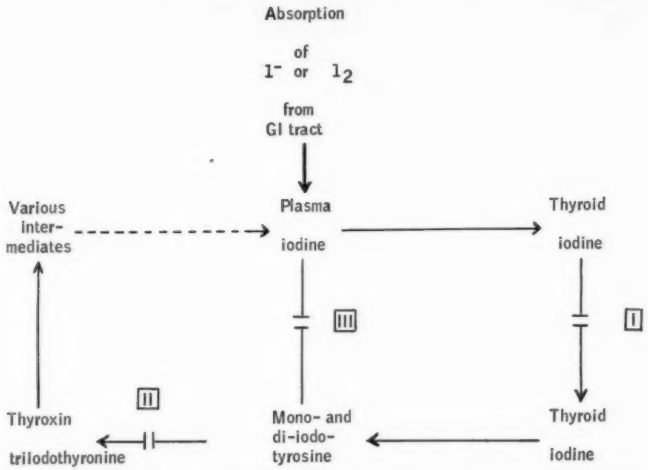

Fig. 47. Biosynthetic pathway of thyroid hormone (postulated). A black at site I results in cretinism from failure of organic iodine to form; at site II in cretinism from failure of iodotyrosines to couple; and at site III in cretinism from failure of iodotyrosine to deiodinate.

tyrosyl residues condense to form iodinated thyronines—namely, thyroxin and triiodothyronine, which are the active hormonal products of the thyroid gland. This coupling process is probably also enzymatically controlled. A defect in this step results in *cretinism from a failure of iodotyrosines to couple.* (5) The remainder of the iodinated tyrosyl residues are dehalogenated by the enzyme iodotyrosine deshalogenase and returned to the thyroid iodide pool. This step is necessary for the proper conservation of iodine in the body. A defect in this system results in *cretinism from a failure of iodotyrosines to deiodinate.*

In order to prevent irreversible mental retardation, treatment of cretinism with adequate thyroid hormone must begin as early as possible. Prognosis of the mental condition in these children depends upon how early treatment is started. There is evidence that at three months an untreated cretin is likely to have sustained permanent mental damage.

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THE LATE CLINICAL SYNDROME OF POSTICTERIC ENCEPHALOPATHY

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The term "kernicterus" was first coined by Schmorl[5] in 1904 to describe the pathologic changes seen in the brains of infants who had died during a siege of neonatal "icterus gravis." The term has recently been extended to include, also, the clinical findings observed in such infants during the neonatal period (first two weeks of life). Such newborns, in addition to the jaundice which begins soon after birth and rapidly deepens, also evince evidence of brain involvement as indicated by a tendency for extensor spasms to occur, with backarching and opisthotonos. The shoulders are held flexed, the elbows extended and the wrists flexed and pronated. In addition, there may be either increased or decreased muscle tone in the intervals between spasms. These spasms may be episodic or at times persistent. After the first two weeks of life these tonic and postural changes are less severe. The general symptom complex is so constant and characteristic in the severely jaundiced infant that it may be stated with confidence that its presence prognosticates that residual symptoms will be seen later in life. There are some who believe that the absence of such symptoms has equal prognostic value in eliminating the possibility that such an infant will exhibit sequelae in later life. When the term "kernicterus" is used in its clinical connotation, it generally is meant to describe the *neonatal symptoms* characteristic of the brain damage of icteric encephalopathy.

Although the jaundice causing posticteric encephalopathy may be due to many factors, the pathologic changes and clinical syndromes which ensue are identical, with few exceptions, regardless of the cause. The advent of exchange transfusions has decreased the incidence of kernicterus due to the Rh factor and to some of the other blood incompatibilities; it has not, however, reduced the total incidence of

kernicterus, which has remained approximately the same as a result of the increase of causes other than the Rh factor. There has been an increase of neonatal jaundice due to other etiologies, as well as an increased incidence of mechanisms inhibitory to pertinent enzyme systems, especially when associated with prematurity or neonatal anoxia. It is true that the appearance of neonatal signs of icteric encephalopathy is almost universally followed by late sequelae in the survivors. The converse, however, is not true, for even in the absence of these neonatal symptoms there may often be unquestionable late sequelae, though often of a milder or more subtle type.

Since the morbid anatomic changes in posticteric encephalopathy are constant and similar, regardless of the cause of jaundice, it is not surprising that the clinical syndromes are likewise rather uniform. In fact, the late clinical sequelae of posticteric encephalopathy are much more pathognomonic than are the neonatal ones. The diagnosis of posticteric encephalopathy can generally be made with more certainty from the later clinical symptoms of the patient than from the early symptoms, which may occur not only in posticteric encephalopathy, but also in edema of the brain, anoxia and other causes of neonatal brain injury. In practically all brains of patients with posticteric encephalopathy there is involvement of the pallidum, hypothalamus, subthalamic nuclei, red zone of the substantia nigra and hippocampus. In most there is also involvement of the dentate and vestibular nuclei and of some of the reticular nuclei. As compared to most of the other clinical types of cerebral palsy, the clinical correlation with anatomic changes is surprisingly good in the syndrome of the late sequelae of posticteric encephalopathy.

THE CLINICAL TETRAD OF POSTICTERIC ENCEPHALOPATHY

The pathognomonic signs and symptoms of the late sequelae of posticteric encephalopathy constitute a readily identified tetrad consisting of (*a*) athetosis, (*b*) gaze palsy, especially of supraversion, (*c*) dental enamel dysplasia, of prenatal or neonatal type, and (*d*) auditory imperception, consisting in hearing loss and/or auditory impressive aphasia.

Athetosis

The presence of athetosis in one of its protean forms is a *sine qua non* for the diagnosis of posticteric encephalopathy. It may at times be mild, at other times severe. Often it may be masked by hypotonia or by the presence of other motor abnormalities, e.g. spasticity or ataxia. Characteristically, the motions are uncontrollable, purposeless, involun-

tary and incoordinate. They may be rapid and jerky (choreiform), slow and wormlike (orthodox athetosis) or so slowed by hypertonicity that the patient may assume momentarily fixed attitudes with stiffness of the extremities (dystonia). There may be windmill-like flailing motions of the arms, especially of the proximal joints (ballismus) or alternate agonist-antagonist movements of the smaller distal muscles (tremors). Any or all of these forms of "extrapyramidal" dyskinesia may exist or coexist in the same patient. One of these types of dyskinesia may predominate at one time or another, so that variability and intermittency of motor defect are characteristic. The amount and nature of the abnormal motion are modulated by emotional factors, sensory stimuli and by the changing status of muscle tone. As the atonic infant gradually develops into the hypertonic teenager, the motor patterns, which remain basically "extrapyramidally" dyskinetic, likewise change in pattern and composition. In all these phases the characteristic usually remains that the motions are involuntary, purposeless and uncontrollable and that the upper extremities are more involved than the lower.

Occasionally the predominating motor abnormality is not that of involuntary motion, but rather "extrapyramidal rigidity" (as differentiated from "decerebrate rigidity," which is physiologically true spasticity). Extrapyramidal rigidity is often intermittently concomitant with athetosis, and only rarely is it a sole and constant finding.

It is true that occasionally the motor defects in posticteric encephalopathy are so mild that reinforcing or special techniques are necessary to elicit them. Even in the absence of any clinical motor defects there may be characteristic residual sensory or perceptual abnormalities, presumably due to minimal pathologic changes in the brain. This is not uncommonly found after exchange transfusions and in patients with posticteric encephalopathy due to factors other than serologic isoimmunization. Nevertheless, the absence of athetosis or of other forms of "extrapyramidal" dyskinesia makes the diagnosis of posticteric encephalopathy dubious, if not untenable.

Gaze Palsy

Palsy of gaze occurs in approximately 90 per cent of patients with posticteric encephalopathy. Although voluntary eye movements in any or all directions may be impeded, palsy of vertical gaze is the most characteristic finding, with greater difficulty in supraversion than in infraversion. The finding of gaze palsy may be difficult to elicit with certainty in the first six months of life, but thereafter it can be elicited with more confidence, provided the child has vision. Characteristically, the patient has difficulty in looking up, but no difficulty in following

objects in the horizontal plane, right or left. When the object he is asked to follow is moved upward, the eyes do not supravert, but the patient first elevates his eyelids and brows and then extends his head in order to keep the object in focus. The same difficulty in following objects may be present in infraversion, but is much less common. At times the difficulty in gaze may be in all directions so that the patient will appear to have a total ophthalmoplegia. It is possible to demonstrate, however, that these are not true paralytic disorders of the extraocular muscles, but represent supranuclear lesions, since all these eye movements may at times be performed involuntarily. In addition, the movement can often be elicited by synkinetic reinforcements. Thus supraversion and infraversion may frequently be elicited by resisting neck extension or flexion respectively, or by alternate passive flexion and extension of the head which may elicit "sleeping-doll eye" movements in the vertical plane. The difficulty in supraversion may vary from complete to only slight degree. As the patient gets older, it spontaneously lessens and eventually may disappear so that this symptom may often be difficult to elicit in the adult.

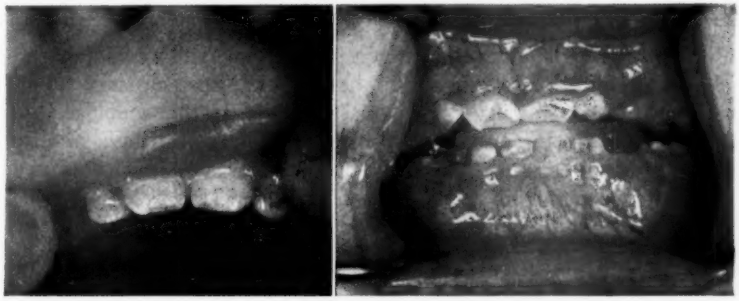
The presence of vertical gaze palsy is much more common in posticteric encephalopathy than in the other types of cerebral palsy. It occurs in practically 90 per cent of those with posticteric encephalopathy, in less than 5 per cent of children with other types of cerebral palsy. Next to athetosis, it is the most constant finding in the tetrad of posticteric encephalopathy.

Dental Enamel Dysplasia

It has long been known that children with posticteric encephalopathy have bad deciduous teeth. For many years this had been attributed to an increased incidence of dental caries and to tooth grinding or bruxism. In recent years, however, the true nature of the dental deficit has become apparent.[3] Basically, the defect consists in a dental enamel hypoplasia of prenatal or neonatal timing. The dental enamel of the deciduous teeth begins to be laid down somewhere between 4 and 4½ months of intrauterine life until birth at a predetermined rate. Because it is laid down in rings much like the rings of a tree, it is possible to use these rings as a calendar for dating lesions. The enamel for the deciduous teeth is fully completed by about the time of birth of a full-term infant so that prenatal dating may be made with a remarkable degree of accuracy, from 4 to 4½ months of intrauterine life until birth. At birth sufficient physiologic disturbance occurs, even in the normal newborn, so that a neonatal line, due to disturbed enameloblast activity, can be recognized microscopically in practically all normal deciduous teeth. The incidence of enamel dysplasia in children with

posticteric encephalopathy is about 75 per cent. Naturally, these findings and their proper dating cannot be done until a sufficient number of deciduous teeth have erupted to reveal these changes. Although the diagnosis can be suspected with eruption of the first few teeth, it may be necessary for 10 or 12 teeth to be present before accurate dating is possible.

Prenatal dental enamel dysplasia is extremely rare in the normal population, while the *neonatal* line may be macroscopically visible in about 7 per cent. In posticteric encephalopathy, tooth ring analysis gives an important hint as to the possible cause of the condition. Prenatal enamel dysplasia is found in nearly 80 per cent of the children with posticteric encephalopathy due to the Rh factor; in this condition



A B

Fig. 48. Prenatal enamel dysplasia and green staining in the deciduous teeth of children with kernicterus due to fetal erythroblastosis caused by Rh incompatibility. A, The enamel dysplasia is moon-shaped and involves primarily the incisors from the tip to a short distance toward the base of the tooth. This region represents enamel laid down between 4½ and 7 months of intrauterine life. B, The green stain in the enamel is intrinsic and can also be dated from approximately the same period. The dyplasia is from 4½ to about 6 months of intrauterine life.

it characteristically involves the dental enamel laid down between 4½ and 7 months before birth. In posticteric encephalopathy due to OAB incompatibility or to most other types of jaundice the dysplasia is more likely to involve the neonatal line. This is suggestive that the injury in the Rh form of posticteric encephalopathy may in some way be initiated between 4½ and 7 months before birth, approximately at the time of rise in maternal antibody titers, whereas in non-Rh posticteric encephalopathy the injury apparently occurs about the time of birth. It should be kept in mind that in non-Rh posticteric encephalopathy, which occurs frequently in prematures, the neonatal line will be recognized after dental eruption, as occurring at a prenatal level commensurate with the degree of prematurity. The only other type of

cerebral palsy in which prenatal dysplasia is commonly seen is in the group of spastic paraplegias and diplegias in whom prematurity is also common.

Another less common finding, but one which is also characteristic of posticteric encephalopathy, is green discoloration of the teeth. This is found more commonly in posticteric encephalopathy due to the Rh factor than in any other types, although it may occasionally be found in the non-Rh cases. It is interesting that the green stain is intrinsic in the enamel and is also generally datable from the period beginning at 4½ to 5 months before birth and extending to about the seventh month and at times even to term. The prenatal defect characteristic of the Rh posticteric encephalopathy may often be seen even in children who have had exchange transfusions and no motor sequelae.

From a clinical viewpoint, prenatal changes are seen most characteristically in the middle incisors, in which there is generally a moon-shaped crescenteric effect, extending from the free edge to a distance about one fourth of the way up to the gums (Fig. 48). In the canine teeth a bandlike defect may be seen just proximal to the tip, giving a noblike or often saber-like appearance to the tooth. When bruxism has caused the teeth to be ground down, these defects may not be visible. The neonatal defect in enamel is found on the incisors at about the level of the gum line and is usually more or less straight. It lies progressively more distal on the more laterally placed teeth. When the gross enamel defects are not visible, microscopic examination of the exfoliated teeth will generally reveal them.

Auditory Imperception

Auditory imperception of some type occurs in over 50 per cent of patients with late sequelae of posticteric encephalopathy. The most common and most easily recognized form is that of a hearing loss of varying degree, from deafness to slight impairment. Characteristically, the greatest loss is in the higher frequencies, so that a "high-pitch cutoff" is common (Fig. 49). Clinically, this may be suspected when the child responds better to the father's voice (generally lower-pitched) than to the mother's, or when he has more difficulty in hearing high-pitched bells or whistles than low-pitched sounds, e.g. airplane motors. In speech, these children often have more trouble in pronouncing the high-frequency sibilant sounds (like "s" or "z") than the lower-frequency guttural ones. They often become adept lip readers without training.

A more subtle form of hearing imperception is that of "word deafness" or impressive auditory aphasia. Although hearing may be normal,

there may be a failure to understand the meaning of words or sounds. When tested by pure tone audiometry, these children may often react as if they were deaf, but normal hearing may be demonstrated by audiometry done with mixed tones or noises of varying intensity and pitch, or by other special techniques such as the electroencephalographic arousal pattern or psychogalvanic response to sound. Such children are often erroneously diagnosed as being deaf because they may not respond to auditory stimuli. The condition may be unrecognized by parents or teachers because the child may frequently respond to sound, particularly when it is reinforced by visual clues. Auditory

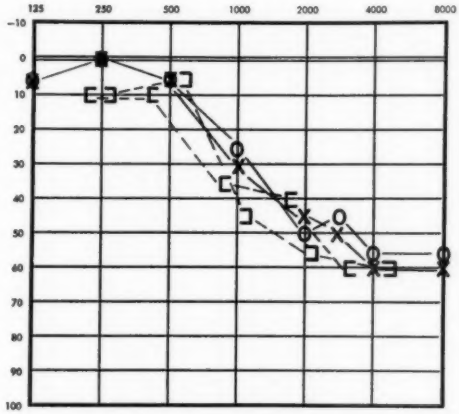


Fig. 49. Audiogram in patient with hearing loss due to posticteric encephalopathy. Note the characteristic greater involvement in the higher frequencies.

imperception of this type is often associated with varying degrees of hearing loss, or may exist alone, to variable degrees. There may be no understanding of language or a limited understanding. The child perceives language much as a normal American child might react to a foreign language, e.g. Russian—it would hear, but not comprehend. If only every fourth word were Russian, the normal child might understand the language better, but still not perfectly. Such children learn better from visual than from auditory clues.

The auditory imperception may often be even more mild or subtle; e.g. only auditory memory may be decreased or distorted. The auditory difficulties of the posticteric encephalopathy patient are characteristic, occurring in about 50 per cent as compared to an incidence of about 8 per cent in nonposticteric encephalopathy athetoids, and 2 per cent in spastics, the same as in the normal population.

ASSOCIATED FINDINGS

Although the tetrad of posticteric encephalopathy is pathognomonic for the clinical syndrome, it is obvious that not *all* of the tetrad may be present or apparent in every patient. If athetosis is present, however, and even only one or two of the remaining three components of the tetrad, the diagnosis of posticteric encephalopathy must be entertained. In addition to the tetrad, other symptoms and associated findings which are present in many brain-injured children, and particularly in the athetoid group, are also seen in the kernicteric child. In order to complete the clinical picture of the syndrome of the late sequelae of posticteric encephalopathy, the associated findings will be described here.

Neuromotor System

The neuromotor symptoms of posticteric encephalopathy and, for that matter, of all athetoids are dependent upon two general characteristics: (1) the nature and degree of the abnormal motion, and (2) the degree of muscle tone which accompanies it. As indicated above, the presence of athetosis or one of its related dyskinesias is a *sine qua non* for the diagnosis of posticteric encephalopathy. There may, however, be other associated abnormalities of motion, e.g. ataxia or spasticity. These must be considered complicating or additional motor defects and not the primary ones for the diagnosis of posticteric encephalopathy. A child who has posticteric encephalopathy associated with prematurity is vulnerable to all the other noxae, in addition to jaundice, to which the premature is susceptible. Since prematurity is frequently associated with spasticity, most severe in the lower extremities (paraplegic or diplegic), it is not surprising that spastic diplegias or paraplegias may often be associated with posticteric encephalopathy of the non-Rh or JAP (jaundice, anoxia, prematurity) type. Likewise, the cerebellar lesions found in posticteric encephalopathy might easily explain the not infrequent association of signs of cerebellar ataxia in these children. Occasionally a child will be found in whom neonatal jaundice existed, but in whom an exchange transfusion was able to prevent the usual motor signs of posticteric encephalopathy. If such a child were now found to have a spastic hemiplegia without any signs of athetosis, the most likely cause would be brain damage due either to the transfusion or to some other etiologic factor, e.g. toxemia, not preventable by exchange transfusions.

The motor involvement is usually so great as to be obvious; at other times it may be so mild as to be virtually unrecognizable except under the broad descriptive terms of being "awkward" or "clumsy." In some instances athetoid motions may become manifest only when the patient

is asked to do a highly skilled act such as writing or cutting with a scissors. They may then be recognized, not only in the fingers, but also in their radiation to shoulder, trunk and even toe muscles. Usually these extraneous motions may be evoked or exaggerated by excitement or emotional stimuli, since it is characteristic of all athetoids that emotional instability increases the athetosis. True athetoid motions are not generally seen in infants before the age of one year, and in mild cases not until 18 to 24 months of age. One may, however, prognosticate that they will appear with almost the same degree of certitude that Koplik's spots herald an impending rash of measles.

These prophetic signs consist in tonic and postural changes in infancy. In the first few months of life the infant exhibits predominant extensor tone instead of the normal predominance of flexor tone (see p. 511). When the shoulders in the supine baby are lifted, there is a decided head-drop. When they are lifted in the prone position, the head is kept well extended. There may be a decrease in muscle tone during the first year of life, but this is primarily in the resting child. During crying or after stimulation there is usually an increase in tone, mainly in the extensors. The tendency is for the arms to be flexed at the shoulders, extended at the elbows and flexed and pronated at the wrists. The legs may react by extension or flexion. As the child learns how to reach and grasp, it is noted that reaching is done with the fingers extended and spread and that flexion of the fingers does not occur until the object touches the palm. Backarching may become a common symptom. As the child grows older, muscle tone generally increases. The degree of muscle tone will determine the nature of the abnormal motion—the less the muscle tone, the more jerky the movements. Tonic neck reflexes may persist for many years, or even throughout life.

From a neurologic viewpoint the child has no abnormal reflexes exclusive of those dealing with tone and posture. Although a startle reflex, a Moro reflex or the tonic neck reflex may be present, the deep tendon reflexes are generally normal; there is no ankle clonus, and the superficial reflexes are likewise normal. It must be pointed out that the neurologic examination of the infant differs from that of the older child or adult (see p. 471). More will be learned from astute observation than from the orthodox neurologic testing techniques. In testing for deep tendon reflexes, the child should be relaxed, a condition best obtained by placing him in the prone position with the knees flexed. In this position the knee jerk is usually not elicited in the relaxed normal or athetoid patient. In the spastic child, however, the knee jerk is readily obtainable. In this position true ankle clonus is likewise more readily obtained. In the athetoid, the "pseudoclonus" often found in the tense patient tends to disappear when he is relaxed. The reverse is true in the spastic, whose true clonus is in-

creased in the relaxed position, but may be inhibited in the tense patient. The extraneous and erratic movements of the athetoid occur most commonly during voluntary effort, associated with lengthening or shortening of muscles. Muscle strength is increased and extraneous motions are decreased when isometric muscle action is attempted as in "muscle setting" or in resisting the movement of muscles. This is opposite of the movement difficulty in ataxics, in whom isometric muscle action is more involved than isotonic action associated with muscle lengthening and shortening.[2] Knowledge of these physiologic characteristics is of value in the treatment of these motor difficulties.

The athetoid generally has good muscular strength and may often have a "Hercules-like" appearance, due to well developed muscles covered by minimal adipose tissue. Since the upper extremities are generally more involved than the lower, the child may walk long before self-help activities of the arm can be accomplished. In some patients with severe athetosis the arms may never have useful function, so that writing and other feats of manual dexterity may be performed better by the feet. The head and neck may be involved in rotatory or extensor-flexor type of motions which may interfere with balance. As can be expected, because of the predilection for greater involvement in the cephalad direction, involvement of speech is common. In some cases, for some inexplicable reason, however, speech may be the least involved function. In the moderately involved case of posticteric encephalopathy, walking is generally accomplished spontaneously, with or without physical therapy or bracing, some time between the fourth and seventh years. Ultimate rehabilitation may be difficult or impossible when the arms and speech are badly involved.

As the child approaches puberty, there may be a spontaneous improvement or regression in the motor symptoms, depending upon the emotional status. Those who are well adjusted seem to improve spontaneously without any treatment. Those who are poorly adjusted and have emotional problems may go downhill in spite of all treatment. This is generally not due to changes in the brain, but is the "pseudo-progression" of puberty associated with emotional lability. A similar progression may also appear at the "Kinsey age" with the waning of sexual life after the age of 40 years.

Ocular Symptoms

In addition to palsy of gaze, there are other ocular symptoms frequently seen in posticteric encephalopathy. Paralytic squint with tropias occurs in less than 20 per cent of the patients, as compared to over 50 per cent of those with spasticity. Esotropia occurs about three times more frequently than exotropia. There is also a refractive characteristic in

posticteric as in nonposticteric athetoids due to anoxia. This consists in a tendency for the physiologic hyperopia of childhood to persist. In normal children, farsightedness, or hyperopia, is normally present in infancy and youth and decreases with age; by the time of puberty, refraction has reached a stage of emmetropia or of slight myopia. In athetoids, including posticteric encephalopathy, there is a tendency for a persistence of hyperopia so that even during the teen ages the child may remain farsighted. It is important to be aware of this, since patients with posticteric encephalopathy generally depend to a much greater degree upon visual than auditory clues. As a result, it may be advisable to correct refractive errors in children with the syndrome of posticteric encephalopathy much earlier than in a normal child with the same degree of hyperopia.

Gastrointestinal Symptoms

There are many gastrointestinal symptoms in the syndrome of posticteric encephalopathy, as in other athetoids. The patient usually has an increase of appetite due to the increased number of extraneous motions. This is similar to the child with Sydenham's chorea, who also may have a voracious appetite and still lose weight. It is therefore not surprising that children with posticteric encephalopathy will consume more calories per pound of body weight than the average child, but in spite of this will be constitutionally inferior. Whereas the normal child in a year will treble its weight, a child with a moderately severe degree of posticteric encephalopathy may do less than double it. Because of the increased nutritional demands, there are also increased demands for vitamins, particularly the B complex. Unless such children are given more than the average daily requirement of vitamins, they may exhibit symptoms of avitaminosis, particularly during periods of severe infection or stress.

The presence of athetoid motions may be associated with persistence of infantile vegetative patterns of the oropharyngeal muscles. Thus tongue-pushing is common, so that a child may have difficulty in sucking and eating, owing to the tendency of the tongue to protrude involuntarily. This may necessitate some special techniques in feeding and may also account, in part, for the malnutrition which is commonly seen. As the child grows older, there is generally some improvement in those involuntary tongue motions. Another interesting pseudoparalytic condition of the tongue is difficulty in voluntary lateralization. The child may have no difficulty in protruding and retracting the tongue, but may be unable to lateralize it upon command. This is similar to the supraversion difficulty of the eye and is of a supranuclear nature.

The muscles which lateralize the tongue are the same as those used in protrusion and retraction, so that true paralysis does not exist. Lateralization of the tongue may be evoked by one of several synkinetic techniques such as unilateral contraction of the masseter or of the orbicularis oculi.

Difficulty in swallowing, as well as a tendency for vomiting, is also a common finding, particularly in the infant. The difficulty may be due to weakness or palsy of pharyngeal muscles or to a spasm of the cricopharyngeus muscle. When the difficulty in swallowing is greater for liquids than for solids, one must suspect the latter condition. There may also be palatal palsy of varying degrees, so that "throwing up through the nose" may not be uncommon. As the children pass the second year of life, the swallowing and vomiting difficulties become progressively less.

There seems to be no particular difference in digestive or gastrointestinal activity in children with posticteric encephalopathy, except the tendency to gaseous distention, constipation and colic. Constipation may be related to highly concentrated feedings, with little roughage, or to the relatively weak abdominal musculature, to the horizontal position and to the tendency for malnutrition and dehydration to occur. The increased respiratory rates, the excessive crying and the superabundance of motion result in excessive moisture loss through the lungs and skin with resultant tendency to constipation. Therefore the children act unhappy, cry a great deal and evince the typical syndrome of the "hypertonic infant." Such findings are not uncommon until about the second or third year of life, when they gradually decrease. Many such children are thought to have food intolerance or food allergies because of this tendency to vomiting, distention and colic. Anal excoriations and fissures are often seen in the severely constipated child.

Cardiorespiratory Symptoms

The patients with posticteric encephalopathy, as well as those with moderately severe degrees of athetosis, generally have a tendency to keep their mouths open. With this abnormal type of breathing it is not surprising that hypertrophied tonsils and adenoids are commonly seen, thus increasing the difficulty of nasal breathing. Stertorous, crowing and noisy breathing is also common in the severely involved infants. This gradually improves with age. The respiratory rate is generally significantly increased above normal. The rate not only is increased, but is also irregular with shallow breathing interspersed with deep breaths and even with periods of apnea. In the severely involved patients there may be "reversed breathing"; i.e. contraction of the

diaphragm may occur during expiration. In normal breathing the chest and abdominal walls move up and down in unison. Reversed breathing may be recognized by the tendency of the abdominal wall to rise as the chest wall is falling. Such a breathing pattern is similar to that seen in Sydenham's chorea (Grave's respiration). The vital capacity is so greatly reduced that the respiratory reserve may be one third or one fourth that of the normal child. There is also a reduced ventilation efficiency, so that roughly twice the volume of air must be respired to utilize each 100 cc. of oxygen. This results in hyperventilation and reduced alveolar pressure of carbon dioxide. Respiratory alkalosis may ensue, which may be responsible for increased muscle irritability, thus initiating a vicious cycle in respiration.

Because of the tendency to strong diaphragmatic contractions, it is not uncommon for a grooving of the ribs to occur similar to the Harrison's groove of the rachitic infant. Likewise, there may be retractions of the manubrium and of the sternum. Other than the tachycardia which is to be expected with increased activity of the athetoid, there are no characteristic cardiac changes.

Orofacial Changes

In addition to the characteristic enamel dysplasia involving the deciduous teeth, other dental changes are commonly seen. Tooth grinding or bruxism is extremely common and may involve all the teeth, but most commonly the upper central incisors. Such wearing down of the teeth may destroy the evidence of prenatal enamel dysplasia. Primary caries does not seem to be more rampant in these children than in the normal, but because of the enamel defects, the bruxism and the high caloric, high carbohydrate diets, these children have secondary caries much more commonly than do the normal. The permanent teeth are generally not so involved. Because of the tendency for tongue-pushing and for the mouth to be kept open, malocclusions and deformities of the jaws are common. Drooling occurs, not because of increased salivation, but because an open mouth makes swallowing difficult. From a clinical viewpoint, one will often note that giving a sucker to such a child will result in increased drooling, since the mouth tends to be kept open and salivation is stimulated, whereas gum chewing may decrease the drooling because of the necessity for closing the mouth more frequently while chewing and thus facilitating swallowing.

The facial expressions associated with laughing or crying are often exaggerated and may be stereotyped with the same response to almost any stimulus. Facial contortions and grimacing are part of the facial athetosis and may often contribute to social ostracism.

Genitourinary Tract Symptoms

There are no characteristic genitourinary changes in these children.

Auditory and Speech Manifestations

The auditory manifestations have already been discussed and will not be repeated. It is of interest, however, that the vestibular portion of the eighth nerve is also frequently involved. The most common vestibular finding is hypofunction of both vestibules to both rotation and caloric stimuli. This finding is not generally reflected clinically. There seems to be little correlation between the degree of incoordination and ataxia of the patient and the amount of vestibular hypofunction. Decreased vestibular function occurs most commonly when there is also involvement of the cochlear portion of the nerve.

As can be expected, speech involvement is extremely common. The difficulties are due to true motor deficits (dysarthrias), particularly of the respiratory and tongue muscles. The respiratory rate is often too rapid for sustained speech; at other times "reversed breathing" due to spasmodic contractions of the diaphragm may interfere with the outflow of air. These respiratory difficulties, in some manner, are related to laryngeal function so that sudden cut-offs in the voice may occur—at times almost like a stutterer. Frequently the difficulty is due to extraneous athetoid motions of the tongue, particularly those controlling motion of the tongue tip. Added to this, there may be difficulty in control of the jaws and the lips, as well as extraneous motions causing torsion and hyperextension of the neck. The mouth may often be held open like that of an opera singer holding a note, except that, as in the stutterer, nothing may emerge but a few grunts. When deafness or auditory imperception exists, there may be disinclination and inability to talk, just as in the deaf. With milder involvement the speech may be garbled and often uneven in intensity and tone. There is generally greater trouble with the high-frequency sibilants when hearing loss is present. In mild cases the speech might be slightly uneven, drawling or awkward. It is surprising, however, that in some patients with rather severe motor involvements there may be relatively little involvement of speech.

Autonomic System

Malfunction of the autonomic nervous system similar to that which occurs in the premature infant is commonly seen. In infancy there may be poor temperature control with a tendency to hyperthermia in the absence of infections, with simple excitement or in the presence of a

warm environmental temperature. For no apparent reason an infant may run a temperature of 104° F. on a hot summer day. In the presence of an infection, e.g. measles, the child may run a temperature 2 or 3 degrees higher than his normal sibling. Increased sweating, flushing and other evidences of autonomic instability are common. Emotional instability is also the rule. Such children will laugh or cry easily. Emotional stimuli will generally increase the athetoid motions. The patient with athetosis due to posticteric encephalopathy is generally not a good poker player, since he is unable to mask the facial evidences of his true feelings. Emotional instability is one of the most important factors in determining the clinical syndrome and the rehabilitation potentials. As the children approach the teen ages, the emotional instability of puberty may be greatly compounded, so that an aggravation of all motor symptoms may occur at this age.

General Constitutional Characteristics

As indicated above, these children generally have a constitutional inferiority as compared to their siblings. They weigh less, are on the average thinner and smaller-boned; however, bone age is normal for the chronologic age. The resulting relatively small stature is often an advantage in that, as the child grows older, the normal group with whom he might be thrown into social contact may be of the same stature, rather than one of the same age, thus making competition easier. Sexual maturation is normal in the mildly involved patients, but may be somewhat delayed in the severely involved. Scoliosis may become evident with the rapid growth of puberty, and particularly in those with asymmetric involvement. The incidence of hip subluxations or dislocations is much higher than in the normal population, though not as great as in the population of spastics.

Intelligence, Mentation and Emotional Responses

Intelligence in children with posticteric encephalopathy is relatively little involved as compared to the motor defect. This dissociation between motor and mental involvement is characteristic. Although some of the most severely involved patients may be feebleminded, as a general rule most of these children are educable. Of the total cerebral-palsied population, the greatest number with superior intelligence is found in the athetoid due to posticteric encephalopathy and in the spastic paraplegias. There is unquestionably some involvement in intelligence, since these children generally have lower I.Q.'s than their normal siblings, but the degree of intellectual involvement is relatively small. Most children with posticteric encephalopathy will walk spon-

taneously by the fifth or seventh year, not only because they have less involvement in the legs than arms, but also because they are generally less involved intellectually than the spastics. Although intelligence as measured by an I.Q. test may not be greatly affected, there is generally involvement of the spectrum of intelligence or of mentation. Perceptual defects, particularly those with auditory components, are common. Visual perceptual defects may also exist, but to less extent. The attention span may be relatively shortened and perseveration may also exist, but to a less degree than in the spastics. There may be hyperactivity, characteristic of the syndrome of the "brain-injured."

In *personality*, the posticteric patient is generally, at least outwardly, different from the spastic. He is much more hyperactive and more aggressive. Unlike the spastic, who often has a masked or "poker" facies, the athetoid smiles and grimaces continuously. This has given the athetoids the reputation of being "extroverts" and "fearless adventurers." Actually, this is not so, for projective tests show that they have the same fears and frustrations as children with other types of cerebral palsy. Their smiles may often be deceptive, since they are often stereotyped without varying emotional content for different stimuli. As the patients approach the teen ages, they may become frustrated and despondent. The suicide rate is higher in this group than in other types of cerebral palsy. Since they have normal mentality and normal feelings, many of them acquire sexual neuroses, perhaps owing to the lack of opportunity for sexual education and exploration available to normal children.

The emotional difficulties are often the greatest deterrent to rehabilitation. Over 80 per cent of those who are unable to find or retain employment are handicapped more by emotional than physical factors. As these patients reach adult life, they either become well adjusted and tend to remove themselves from the social classification of the "cerebral palsied," living useful and happy lives, or they become more emotionally agitated with "pseudoprogression" of their physical disability, leading to institutionalization or premature death. The death rate among this group may be 10 to 15 times that of the normal population of the same age.

Seizures and Electroencephalograms

Seizures are much less common in the posticteric than in the other forms of cerebral palsy. In the first two to four weeks of life there may be extensor spasms which might simulate or be classified as seizures. The tendency is for these to disappear, however, after the first month of life. During infancy this group might have more febrile seizures than the population of normal infants. After the second year of life, how-

ever, recurrent seizures are much less common than in the spastic forms of cerebral palsy. Whereas seizures occur in over 50 per cent of the spastic patients, they occur in less than 20 per cent of those with posticteric encephalopathy. The electroencephalograms are likewise more likely to be normal in this type of cerebral palsy than in spasticity. In the cerebral-palsied children who have recurrent seizures the incidence of abnormal electroencephalograms is about 90 per cent; in those without a history of seizures the presence of a normal electroencephalogram weights the evidence two-to-one that the patient is likely to be an athetoid, rather than a spastic.[4]

Electromyographic Patterns

Electromyography is not too helpful in differentiating the athetoid from other forms of cerebral palsy. At rest there is usually silence with some periods of spontaneous activity in the agonist muscles and primarily in those which are most involved, e.g. the upper extremities. No abnormal potentials are found. The patterns of activity, however, differ from that in spastics, in whom the radiation of activity is to the antagonist and synergist muscles in predetermined patterns. In athetoids, on the other hand, radiation is primarily to the muscles most involved with athetosis, as indicated by electromyographic activity at rest. The pattern is thus one of channelization of the spread of activity to a specific area, differing for each patient.[6]

Rehabilitation Potentials

The rehabilitation potential of the patient with posticteric encephalopathy naturally varies with the severity of the disease. In patients who are severely involved these potentials may be greatly reduced, since the arms are generally more involved than the legs and since rehabilitation potentials are much more dependent upon arm than leg function. In patients with mild sequelae following posticteric encephalopathy the involvement may be so slight that no treatment is necessary to assure employability. This is true in approximately 25 per cent of the patients in this group. In another 25 per cent the severity of involvement is so great that no amount of training will ever rehabilitate the patient to even the point of self-help. In spite of good intelligence in many of this group, the degree of physical handicap may preclude the ability of the patient either to care for his own needs or to hold any type of job. The remaining 50 per cent are moderately involved patients in whom some degree of rehabilitation may be achieved, if not to the point of employability and independence, then at least to some degree of self-help. Rehabilitation of this type of patient is more difficult than that

of the spastic of a similar degree of involvement because in posticteric encephalopathy, as in all athetoids, there is greater involvement of the arms. In the group of moderately involved patients the rehabilitation potentials may be more dependent upon emotional than upon physical handicaps. This is why cognizance of emotional factors is important from the moment the diagnosis of the disability is made.

Management, which generally involves parental counseling, should be started early in life. The language difficulties of these patients, as well as their general appearance, e.g. drooling or grimacing to a grotesque degree, may also be factors in posing social impediments. For this reason rehabilitation programs are often more successful if initiated in sheltered workshops or in rural projects such as farming.

NATURAL HISTORY OF THE DISEASE

In all areas of clinical medicine it is necessary to have knowledge of the natural history of a given disease in order to prognosticate more accurately and to anticipate and thus possibly forestall deleterious occurrences, and to assess the possible value attributable to therapy. Although a description of the natural history of posticteric encephalopathy may be repetitious of some of the items mentioned in the inventory by systems, it may be worth while, in order to place some of these symptoms in their proper perspective.

The history of jaundice in any newborn should alert the doctor to the possibility that there may be some clinical sequelae in later life, associated with this etiology. The statement that it takes an indirect bilirubin serum level of 20 to 30 mg. per 100 ml. to cause kernicterus is not entirely correct. It may be that at levels below this, the symptoms of *neonatal* syndromes of kernicterus may not be evident or that the more obvious sequelae of posticteric encephalopathy may not exist, but more subtle sequelae such as auditory imperception may ensue and be recognized in later life. Although there is great correlation between the serum levels of bilirubin and clinical sequelae in patients in whom the Rh factor or other isoimmunizations occur, this is not nearly so true of children in whom the jaundice may be due to other causes such as the kernicterus of JAP (jaundice, anoxia, prematurity) or in jaundice due to depression or immaturity of the enzyme systems involved in the detoxification of indirect bilirubin. From a clinical viewpoint, therefore, one must recognize that the natural history of posticteric encephalopathy will vary with the severity of the condition, whether mild, moderate or severe. Naturally such a classification of severity does not represent a trichotomy, but rather clinical aggregates in a continuum of syndromes.

In patients with mild involvement there may be no symptoms other

than the jaundice in the neonatal period. In about 10 per cent of the patients even this history is not obtained, perhaps owing in part to human inadequacies in observation, but unquestionably in part to the fact that the clinical syndrome of posticteric encephalopathy may be duplicated by anoxia in a premature or other debilitated infant, even in the absence of visible jaundice. This is but further evidence of the fact that the clinical syndrome of posticteric encephalopathy is not, itself, an exclusively defined and delimited condition, but is also a portion of the continuous spectrum of brain injury due to anoxia in its broadest sense. From a pathologic viewpoint the brain lesions due to anoxia may closely resemble, in location as well as in histology, many of the findings in posticteric encephalopathy. During infancy and young childhood there may be no or only minor symptoms in the mild cases. There may be a history of failure to gain weight in spite of a good appetite or of some delay in the acquisition of speech. As the child begins to walk and use his hands more, he may be accused of being a little "awkward" or "clumsy." Frequently the parents feel he is "nervous" because there is some degree of hyperactivity, greater during excitement or aggravation. It may not be until he begins school that some difficulty is noted in oral reading or in those spheres of education dependent primarily upon auditory adequacy. As the patient reaches the teen age, his "awkwardness" and his school difficulties may result in emotional and behavioral problems. In order to understand and to combat these difficulties, the clinician should be alerted to the possibility that they may represent mild or forme frustes types of posticteric encephalopathy.

In patients who have somewhat more involvement the clinical evidence of kernicterus, so characteristic of the first two weeks of life, may be evident. There may be varying degrees of backarching, with arm extension and pronation during the first two or three weeks of life. After this period there will be changes in muscle tone, characterized by a continuation of the hypertonicity, but more often by hypotonicity. During the first six months of life the patient with posticteric encephalopathy may exhibit the syndrome of the hypertonic infant with continuous discomfort, crying, constipation, distention and backarching.

When hypotonicity of the muscles predominates it gradually decreases with age. The tonic neck reflexes may persist beyond the sixth month of life or for variable periods of time. The Moro and startle reflexes may also be evident for many years. These children have excellent, often voracious, appetites, usually better than those of their siblings, but are generally physically inferior in height and weight. Temperature lability and a tendency to run higher temperatures than their siblings do during acute infections may be present. Febrile seizures or breath-holding spells may also be more common. Acquisition of speech will often be determined by the presence or absence of auditory in-

volvement. True athetoid motions may not become manifest until the child is 18 or 24 months old. One can predict that they will appear by noting the abnormalities in tone and posture which antedate the appearance of athetoid motions. When grasping attempts appear, they are characterized by a tendency for the fingers to be kept extended until the palm is touched. After the age of two the athetoid motions will become more and more manifest, both during times of rest and during attempts at voluntary motion. By the time the child has reached six years of age he is likely to be walking without help and without bracing.

The gait of the child with posticteric encephalopathy is characterized by the presence of an extensor thrust, strongest at the ankles. This may result in toe-walking for a longer period than in a normal child. Unlike a spastic, however, there is little tendency for tightening of the heel cord. In some children in whom both heel and toe touch the floor, the extensor thrust may cause a genu recurvatum at the knees with a lordotic and abducted position of the hips. They tend to waddle as they walk. Since shoulder athetosis is greater than that at the hips, sudden athetotic jerking of the shoulders or neck may throw the patient off balance. Most of these patients tend to fall backwards, although they may overcompensate and thus fall forward. Generally, the involvement is quadriplegic, although one side is a little more involved than the other. At times there may be greater shoulder involvement on one side and greater involvement of the hands on the other. This may result in confused handedness with a predilection to reach with the arm with better shoulder function, but to do skilled acts with the fingers of the hand with least involvement.

As the children grow older and start their school work, whether in classes with normal children or with those with physical handicaps, the problems of education and communication become paramount. This, of course, is dependent upon the amount of speech, hearing and auditory perceptive involvement. These children may drool and grimace a great deal, and their general performance may be more dependent upon their emotional than their physical status. It is necessary for their proper ego development to proceed from the stage of full dependence on adults, especially parents, during infancy and early childhood, to a stage of complete independence by the time they reach the teen age. Unless parents and teachers are cognizant of these needs, there may be overprotection and infantilization or too many frustrating experiences as a result of aiming at unattainable goals. As a result, puberty may be associated with exaggerated emotional involvement which may cause progressive advancement of the motor defects, the so-called "pseudoprogression of puberty."

Because of the relatively good intelligence, a great many of these patients may continue their education into college and higher degrees.

Unless there is good practical planning for their future, they may end up as misplaced and frustrated Ph.D.'s. Many, however, may lead perfectly normal lives. They may marry and raise families. The longevity in this group of patients is about 45 years, which is much less than in the normal population, which reaches an average age of 67 to 70 years. Alcoholic habituation is not uncommon in this group of adults, since they learn rather early that the best tranquilizer is still alcohol and that they feel and perform better after imbibing an alcoholic beverage.

In patients who have severe involvement there is an exaggeration of all the symptoms seen in the moderately involved patients. For the first two to three weeks of life they may have continuous extensor spasms and, in addition, may have focal seizures, as well as some grand mal. These extensor spasms may last for many months. After the fourth to sixth week of life decreased muscle tone may be the predominant symptom, at times being so great that the myopathies may be simulated. The important difference between amyotonia congenita and posticteric encephalopathy in the first three to six months of life, however, is that in amyotonia congenita there is generally an absence of the deep reflexes with equal weakness in the flexors and extensors of the body, and with an inability of the patient to increase his tone noticeably during crying or after other stimuli. In the patient with posticteric encephalopathy, however, knee jerks will often be elicited, especially by reinforcement techniques, and the weakness of the flexors of the trunk and head is much greater than that of the extensors, which may be normal or may actually be hypertonic in response to sensory and emotional stimuli. The hypotonia at rest, which is commonly seen, may remain until the sixth or seventh year of life or even longer. Generally it is replaced by hypertonia by the time the child reaches the teen age. During infancy there is likely to be greater involvement of the thermal centers, unexplained fevers occurring on hot days, and the syndrome of the hypertonic infant is much more common. Difficulty in swallowing and retaining food may occur. Sometimes these children can be fed best in the prone position.

In spite of poor nutrition and poor tissue turgor, the muscles may be highly developed, giving the patient a "Hercules-like" appearance. When there is hypertonicity, however, the muscles are entirely relaxed during periods of sleep or even when the patient is awake but comfortable. Unless there is excessive backarching, many such children will be more comfortable on their stomachs than on their backs. Tooth grinding and caries are common, as are malocclusions. Constitutional inferiority, in spite of voracious appetites, is the rule. In these children extrapyramidal rigidity, as well as other dyskinetic symptoms and superimposed spasticity, is commonly found. There may be retention of the

tonic neck reflexes throughout life. Seizures and abnormal electroencephalograms are more common in this group. Although intelligence is also more likely to be decreased than in the patients with less severe motor involvement, it is sometimes surprising how good the intelligence may be in such a patient in spite of the severe motor involvement. Hand function may never be attained, so that attempts at writing or typing may be done better with the feet or with implements held in the mouth, or strapped to the forehead. Usable speech may never be attainable, but, again it is sometimes surprising that good speech may exist in spite of the severe physical disability. In this group, contractures may occur because of enforced and continuous sitting and because of extreme and often unbalanced hyperactivity of muscle groups. Such contractures, however, are not generally severe until after the eighth year of life. The extraneous motions may be so great and violent as to cause subluxations or dislocation of the hips and of the shoulders. These patients may never ambulate on their own and are generally not amenable to any degree of useful rehabilitation.

As in all fields of medicine, there will be variations in the configurations and patterns of symptoms that make up a given clinical syndrome. To the clinician, it is not necessary that every patient exhibit every known symptom characteristic of a disease in order to make a diagnosis and to treat it. Although there are no two patients with posticteric encephalopathy who are clinically identical, they all have so many symptoms in common that the syndrome of the late sequelae of posticteric encephalopathy can be considered an entity. Recognition of such an entity not only allows one a better understanding of the pathogenesis of the condition, but also throws light on its relation to other injuries of the brain.

Cerebral palsy is not a specific condition, but is composed of a group of clinical entities, each with characteristic causes and symptoms. The late syndrome of posticteric encephalopathy is one of the few such entities in the cerebral-palsied group in which there is excellent correlation between etiology, pathogenesis, pathology and clinical symptomatology.

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TUMORS OF THE CENTRAL NERVOUS SYSTEM IN CHILDREN

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Specific histologic details of brain tumors in children and details of operative technique may be found in a variety of sources.[1, 2, 3] I am more interested here in material which can help the pediatrician understand the neurosurgeon and interpret the situation to the family of the patient. Furthermore, the assistance the pediatrician can give in preoperative and postoperative care of the child can be significant.

BRAIN TUMORS

Symptoms

When should a brain tumor be suspected? Whenever a symptom which could possibly be due to tumor persists and cannot be explained on the basis of some other disorder. Perhaps the most confusing symptom is *vomiting*, especially that which occurs soon after the child has arisen in the morning and then does not recur during the rest of the day. It is remarkable that appetite is often not impaired, and the child may well eat a second breakfast without difficulty, and spend the rest of the day comfortably. The vomiting is particularly difficult to understand because it may be unaccompanied by other symptoms. When the child is of beginning school age, an emotional cause may be suspected, concerned with leaving home, or some such reason. It has happened that a considerable gastrointestinal investigation may be instigated by such morning vomiting, only to have the central origin turn up in time. Since brain tumor is much less common than other causes of vomiting, perhaps the head should not be investigated first, but if no enteritis, ulcer or other gastrointestinal cause is evident, then neurologic investigation with skull x-rays may well prove useful.

There is nothing specific about the *headache* of early brain tumor, except that it may be related to vomiting or another symptom. It is not localized and reproducible by tapping the forehead or cheeks, as is true of sinus infections. Visual symptoms may accompany brain tumor, or headache may be of ophthalmologic origin, for which reason eye investigation may well be a part of the study of a child with headache. It may be easier, in fact, for the ophthalmologist to see the eyegrounds and to map the visual fields than for the pediatrician to do so; however, any doctor may have trouble with these examinations. Even 7- and 8-year-olds may be unable to keep their eyes still enough for funduscopy, in spite of mydriatics. Nevertheless, mydriatics should certainly be used if the physician is to track down the cause of the trouble. In smaller children rectal Seconal or other sedative may well be indicated. Such scrupulous eye examinations must be done with presenting complaints that have to do with the eyes; blurred and double vision in particular should be the warning signals. To me, optometrists have no part to play in the care of the eyes of a child, and especially not for the initial investigation. At times the child's visual difficulties may not be verbalized, and the parent becomes aware of the trouble only when the child begins to bump into things.

This was true of the 3-year-old boy who was recently hospitalized for failing vision. He had started to stumble at two, was examined by a pediatrician who sent him to an ophthalmologist who made a diagnosis of optic atrophy, and told the parents there was nothing to be done about it. Six or 8 months later the parents did go to another ophthalmologist, who confirmed the diagnosis of atrophy and sent the child to a second pediatrician for further study. In the year which had elapsed from the first visit to the doctor, no further x-ray pictures were taken. The original films showed the virtually pathognomonic undermining of the anterior clinoid processes indicating glioma of the optic chiasm.

Differentiation between strabismus of developmental origin and that due to intracranial cause is too important to be left to anyone but a skilled ophthalmologist.

Many brain tumors (60 to 75 per cent, depending on choice of references) are in the posterior fossa and involve the cerebellum, so that it should be no surprise to find *incoordination* a common symptom. Staggering, unsteady or broad-based gait should always lead to suspicion of tumor. Sometimes the incoordination is also found in one arm or leg; at times it is best seen in inability of the seated child to hold himself erect (so-called truncal ataxia). Sometimes falling to one side is associated with tilting of the head to one side or the other—such a "torticollis" may be thought due to disturbance in the cervical spine and lead to misplaced interest. It is a phenomenon ascribed to reflex mechanisms which open an intervertebral foramen or to spasm which prevents painful movement.

Unilateral *weakness* of one or both extremities is usually of gradual

onset when a cerebral tumor grows in a child. Sometimes it occurs with vomiting, headache, stiff neck and mild temperature elevation, and can be confused with encephalitis or poliomyelitis (which rarely affect arm and leg at the same time). Associated symptoms, history and examination should make the differential diagnosis possible.

Convulsions may occur for the first time with fever from upper respiratory tract infection in childhood, and may indicate "merely" the presence of abnormally sensitive brain cells. They may also indicate brain tumor, however. This is especially to be investigated when there is a focal sign to the convulsion. Anticonvulsant medication may be given while the nervous system is being investigated. The neurologic side effects of hydantoins (such as Dilantin) mimic cerebellar dysfunction, with which there are rarely convulsions, so that the effects of medication need not be confusing.

Apparent *endocrine dysfunction* in prepuberal children is so common that the lack of gonadal development produced by craniopharyngioma may not be striking. Precocious puberty is more commonly due to some disorder other than pineal tumor, but the association is so striking (when it occurs) that tumor of the brain must be investigated whenever sexual maturation is decidedly premature. I have not seen precocity due to brain tumor in girls.

Signs

What kinds of examination are indicated when a brain tumor is suspected? Those which will lead to diagnosis (if one is possible). Sometimes a good neurologic examination can lead to an accurate diagnosis. The combination of headache, vomiting, staggering gait, nystagmus and papilledema has been enough, in the past, to lead to operation for cerebellar tumor, although today some accessory examination is certain to be done. The examination can be done, in the first instance, by the family physician, be he (or she) pediatrician, internist, generalist, or other. Those less certain of their techniques may seek more expert help from the neurologist, especially if the findings are not immediately conclusive for tumor. If they are, the neurosurgeon may be called in immediately (depending on local "interpersonal relationships").

Sixth nerve paralysis, or less commonly third nerve paralysis, should be readily observed if it is present. If there is doubt, ophthalmologic consultation will be needed. If the fundi can be visualized, papilledema may be evident (in as high as 50 to 75 per cent of the patients). Nystagmus may be present in a third of the patients, and optic atrophy in about a tenth. Staggering gait, ataxia in finger-to-nose or heel-to-knee tests, incoordination in rapid alternating movements and other signs of cerebellar dysfunction are common. Discrepancy between "tendon"

reflexes between the two sides, Babinski signs in children over age two years, loss of muscle power in arm and leg are other significant signs.

Accessory Diagnostic Investigations

X-ray films of the chest and skull certainly may not be dispensed with in modern medical practice. Metastatic tumor to the brain is not common in children, but it would be unfortunate to miss tumor deposits in the lung, and tuberculosis of the chest and brain does still occur in the United States (as well as in other countries). Most of the time the most striking change in the *x-ray of the skull* is separation of the cranial sutures. This indication of increased pressure may be accompanied by pressure changes in the remainder of the calvarium (so-called beaten silver appearance); however, the occurrence of this local thinning of the bones of the cranium *without* suture separation has no significance. It does not, of itself, indicate generalized increase in intracranial pressure. The interpretation of early suture separation in children below age four or five may be exceedingly difficult, and may ultimately depend on some accessory investigation (such as papilledema or elevated cerebrospinal fluid pressure). It does help for the radiologist or neurologist to have access to a series of films of normal children of various ages. Erosion of the sella turcica does occur with sustained intracranial hypertension in children (as it may in adults). Consequently, such a change in the base of the skull should not be thought due to pituitary tumor, which is rare in children.

J.H., 10, was sent home from school because of too-frequent visits to the bathroom. The physician had x-rays of the skull taken, disclosing erosion of the sella turcica, and referred the child for "pituitary tumor causing diabetes insipidus." The same x-ray films showed multiple calcifications in the region of the pineal body, and ventriculography showed the filling defect due to a pineal tumor. The elevated intracranial pressure responsible for the pressure on the floor of the hypothalamus (and the diabetes insipidus) was relieved by a Torkildsen's cisternoventriculostomy.

Calcifications must be searched for in x-ray studies of the skull, for they may give the diagnosis with considerable accuracy (as with craniopharyngioma). But absence of calcification does not mean absence of such a tumor. Calcifications of non-neoplastic origin are commonly multiple (as in tuberous sclerosis, toxoplasmosis, hypocalcemia, and so on). *The film quality must be of diagnostic quality*—i.e. the exposure must be adequate to allow visualization of calcification and of sutures. The most common fault is underexposure, with resulting whitish films. Movement is just as troublesome, especially with small children, and appropriate restraining bands should be available (to save the technician's hands from exposure incurred while holding the head). As with ophthalmoscopy, so with radiology: better results may be obtained with appropriate sedation of the child. When postero-

anterior films are difficult to take because of the face-down position, upright or across-the-table films with a screen grid may be helpful.

There may be considerable reluctance to subject a child to a *lumbar puncture* as an office procedure, with some justification. This is an important diagnostic aid, and should not be attempted casually. Sedation should be used in all small children, and in many others under the age of 10 or 12, depending on the personality characteristics of the child. Here the pediatrician can help in giving some estimate as to the success of such a procedure. Probably the puncture should be done in the hospital, for in the work-up of a brain tumor suspect this can be a major factor in diagnosis. Restraint sheet, proper holding technique, local anesthesia (often after local spot freezing with ethyl chloride) and skillful operator are all essential. Lumbar puncture in children should not be turned over to a new interne, nor to anyone not well trained.

In my opinion no lumbar puncture should ever be done without using a water manometer to measure the pressure. There are so many factors which determine the rate of drop formation besides pressure that any estimate of pressure from rapidity of the flow can be only a guess. In a high percentage of children an accurate pressure reading can be made if the puncturer is willing to wait until the struggling and crying calm down. A safe rule of thumb is that no fluid should be removed (except that which is in the manometer) if the pressure is over 200 mm. of water. There is a current campaign to promote "careful" lumbar puncture in the presence of papilledema, and the incidence of complications may well be small—but complications do occur if fluid is removed from below a cerebellar mass. One needs only to see one autopsy provoked by such a procedure, in a child with an operable posterior fossa lesion, to change his opinion as to the safety of this procedure. Naturally, if in seeking cerebrospinal fluid in a case of presumed brain tumor one finds true subarachnoid bleeding or the cloudy fluid of meningitis, these strictures about removing fluid do not hold, for then there is no ball-valve mass to move about so dangerously.

Occasionally it is difficult to do a spinal puncture in the lateral decubitus position, and a sitting puncture is done. Reports of cerebrospinal fluid pressure should then specify this, for the normal sitting pressure may be considerably variable (with the height of the child, especially). In general, pressures at or below the level of the foramen magnum are normal.

If the pressure is normal, fluid is removed for study, particularly of the cells, protein, serology and gold curve. Chloride and glucose determinations are rarely of importance except with infections. Cell counts may be increased with tumors, and it is wise, when fluid is available, and cells are increased beyond 10, to ask for Papanicolaou

smears. Occasionally these can be of great value in determining future course of procedure (as in deciding whether biopsy shall be done on a dangerously situated tumor). It does no good whatsoever to compress the jugular veins in Queckenstedt's maneuver in a patient suspected of having a brain tumor. It is possible, if the pressure is already high, to cause more trouble, and beneficial information is not likely to be obtained.

Sometimes the combination of neurologic examination, x-ray study and cerebrospinal fluid investigation is adequately diagnostic to permit operation (e.g. craniopharyngioma with calcification). More often, however, some other test needs to be done. Which shall it be?

The *electroencephalogram* is easiest of the commonly performed accessory studies. It is particularly valuable when convulsions are a prominent part of the symptomatology. However, it is of no value in the diagnosis of posterior fossa tumors. In cerebral tumors the electroencephalogram may be accurate in perhaps 60 to 70 per cent of cases, being of least value in midline masses. Most neurosurgeons use this test as a screening maneuver in early diagnostic attempts, when additional impetus is needed to push the referring physician or the family to permit one of the more accurately diagnostic techniques.

Air studies are the most valuable, with a diagnostic accuracy for *ventriculograms* of about 95 per cent. There is an increasing use of *pneumoencephalography* in suspected brain tumors, with removal of little or no fluid when a tumor producing elevated pressure is present. This hazardous procedure is naturally done only by experienced personnel, usually with the operating room already prepared for the forthcoming procedure, and frequently only after preparatory burr holes have been made in case of trouble. In either event it is commonly accepted that when an air study shows a tumor in the presence of elevated intracranial pressure, operation should immediately follow—or at least that the air should be evacuated again, for if it is allowed to remain in place, the condition of the patient may rapidly deteriorate. With lesions near the posterior end of the third ventricle, which may not permit proper visualization by air study, it is sometimes useful to inject Pantopaque or Lipiodol and manipulate the head under x-ray guidance to obtain pictures of the opaque material flowing through the ventricular system.

Carotid and vertebral *angiography* is sometimes performed in children, especially if there is a question of differentiation between vascular and neoplastic disease. The procedure in children is usually done under general anesthesia, and ordinarily does not carry the impelling need for immediate operation that air study may. Technical difficulties involved in cannulation of small arteries in children may be influential in choice of these tests. They have somewhat less accuracy (over-all) than air

tests, but when diagnostic may carry also a preoperative prediction as to extent and type of neoplasm (as in meningiomas).

Radioactive isotope uptake by tumors permits a painless technique of adding information in some cases. The equipment and technique are not standardized, nor is there agreement on the diagnostic validity of the results. The benefits are least apparent with tumors of the midline and those of the posterior fossa, which together constitute the majority of brain tumors in children.

Treatment

What treatment shall be used? Except when metastasis from a known primary tumor is evident, operation is usually the first choice. *Radiation therapy* alone is rarely indicated without biopsy or procedure designed to overcome elevated intracranial pressure. Thus pineal tumors may well be left undisturbed, but their strategic location, blocking the aqueduct, makes it necessary to do some bypass operation before radiation can be used.

Operations for brain tumor have several functions: to obtain a piece of tumor for diagnosis, to relieve pressure, or to remove the mass lesion. Sometimes all these objectives are achieved, sometimes only one, and, unfortunately, sometimes none. Some tumors are so situated that they cannot be removed without immediate death of the patient; others are strategically located so that removal results in paralysis or blindness, or some other handicap. When radical surgery should be done is still largely a matter of opinion, based on morals and ethics (e.g. hemispherectomy for deep-lying astrocytoma in a child who has had only several focal convulsions). Most neurosurgeons *try* not to inflict more impairment of function, preferring to make a biopsy or partial removal and then to follow with x-ray therapy. Sometimes such a course of events is the only proper one, as in ependymoma arising from the medulla oblongata. Sometimes a total removal can be made, as with cystic astrocytoma of a cerebellar hemisphere. Usually no preoperative estimate can be given as to whether a tumor can be totally removed—and sometimes discretion dictates partial removal, careful histologic study, and a later, second operation.

Postoperative radiation all too often represents a last-ditch effort, a means of equivocation with the admission that medical science or technology has failed (as is true with most pontine gliomas). Sometimes it is the effective means of postponing disaster for months or even several years, as when it is given to the skull and spine after operations for medulloblastoma.

Chemical treatment of brain tumors in children has not yet proved effective. The occasional report or rumor of improvement following

one agent or another has to be balanced against the equally rare occurrence in which spontaneous subsidence of a neoplasm takes place. The philosophy usually has been: What is there to lose? The attitude of the neurosurgeon usually depends on his personal involvement: most of the time he will have nothing to do with the "unacceptable" medication. It is the family doctor who has the burden of dealing with the family who will leave no stone unturned, and who will gladly shift the load to the experimenter. In light of the occasional success with cortisone and its analogs in slowing down the progress of metastases from breast carcinoma, perhaps this avenue should be more explored with children, too.

The pediatrician in private practice usually should be invited by the neurosurgeon to help care for the child before and after operation, since the problems of fluid balance in particular are so knotty in children. Administration of sufficient fluids and electrolytes and blood before operation can make the child a better operative risk. Preoperative use of cortisone has radically altered the postoperative course of children with lesions in the region of the hypothalamus. It is rare now not to give blood during operation for brain tumor in children, and to ensure an unimpaired flow, infusion in a malleolar vein is common. Other infusions are needed, too, for the fluids given by the anesthesiologist, including recently 25 to 30 per cent urea as a dehydrating agent. The brain shrinkage with this material may give sufficient space to make the difference between failure and success in operation, especially near the base of the brain. The complications of its use are few, especially if care is used to gradually rehydrate the patient.

Among the recent helps in neurologic surgery are Arfonad (trimethaphan camphorsulfonate) and hypothermia. Both are particularly useful in management of vascular lesions (meningiomas, arteriovenous malformations) by dropping the blood pressure to minimize blood loss, and by protecting the cerebrum against the ill effects of ischemia. Postoperative care is necessarily meticulous, to prevent cardiac irregularities, rebound hyperthermia, and other complications.

Most parents want to know some of the outlines of how a cranial procedure is done, and the best analogy is usually that of the making of a trapdoor which is later replaced. When bone must be permanently removed, as in decompressive procedures or in posterior fossa explorations, the parents must be told. Almost always there is sufficient muscle overlying the area of bony removal to afford adequate protection.

There may be much anxiety about hair loss, so that reassurance is needed about rapid regrowth (except when radiation therapy is to be given, and then this matter is discussed at the time when the therapy is instituted). It may be well to save the hair removed before operation, but it should not be given to the relatives with the injunction to

save it in case the patient dies (as is recorded in a recent popular magazine article). If it is asked for later, then it can be handed over. To avoid the difficulties and dangers from contamination of the incision by hair, it is preferable to have the entire head clipped and the region of operation shaved. For small children the shaving certainly should be done when the patient is asleep.

Concern is also evinced about postoperative activity of the child so far as the head is concerned. If a bone flap has been turned and replaced with sutures through the bone, there need be no fear of the child's lying on this part of the head, and ordinary play activity should be possible within three months. Head-contact sports should certainly be delayed for at least a year. When a decompression has been left, and there is bulging, the nature of the swelling must be explained, and precautions for protection given (most of the time these include only avoidance of direct pressure from hats, and the like). The ordinary weight of the head lying on a temporal decompression is usually not distressing to the patient. Later the decompression may become depressed, or may fluctuate, with some concern to the parents if they are not told of the safety valve function of this area. When a bone flap must be sacrificed and the tumor has been completely removed, replacement may be done at a later date—with the patient's own or banked bone, plastic or metal. When the bone is lost because of later osteomyelitis, regeneration of the bone often occurs surprisingly well.

Convulsions may occur after operations on the cerebrum even when none occurred before. Judgment of the individual neurosurgeon dictates whether these are likely enough to warrant warning the parents. In many instances it is worth while to put the child on an anticonvulsant (such as phenobarbital or a hydantoin) for several months and then gradually withdraw it to minimize the possibility of convulsions in the early, anxiety-ridden months after operation. Certainly if convulsions preceded operation, anticonvulsants should be administered for six months after operation, and then only gradually withdrawn if clinical course and electroencephalogram indicate the possibility of nonrecurrence.

Prognosis

It remains unfortunately true that most children with brain tumors cannot be cured. The prognosis varies with the type and location of the tumor. It is not possible to give anything but a general guess as to the future in most cases. The most common tumors of the posterior fossa are the ependymomas and medulloblastomas, which respond promptly but incompletely to radiation therapy: when they recur, reoperation is rarely effective, especially if there are metastases elsewhere.

The length of life is usually less than two years. Cerebellar astrocytomas have a better prognosis and, when cystic, may be completely eradicated. When they are solid, complete removal of the tumor may not be possible, but the child may live for several years, and then reoperation may be done, so that survival periods of 5 to 10 years are not rare. Glioblastomas, more commonly found in the cerebral hemispheres, are invariably malignant and cause death within a year. Cystic astrocytomas of the cerebrum may be curable if a mural nodule can be removed. Solid ones may be removed if they are in frontal or temporal lobes, and there may be less hesitation in removing them on the left in young children, since permanent aphasia from left-sided damage is rare in children under 12 (owing to education of the right cerebral hemisphere). Craniopharyngiomas rarely can be totally removed, but when they are cystic, removal of the oily contents may be followed for some years by improvement, and reoperation may be done. Midline spongioblastomas of the third ventricle or pons may be compatible with life for several years and, in rare instances, seem to be inhibited for many years after radiation therapy. When hemispherectomy has been done for hemisphere tumor, survival may be possible, albeit at the cost of a considerable neurologic deficit.

The statistics for survival of brain tumor patients are not worse than those for children with cancerous growths elsewhere. Early diagnosis and treatment are still urgent, for there is no prediction in advance that the tumor is to be inoperable or malignant, and with more radical treatment and the newer aids to operation, more and better survivals will occur.

TUMORS OF THE SPINAL CORD

Spinal cord tumors in children are much less common than brain tumors. The principal *symptoms* include gait disturbances, weakness of the legs, clumsiness, pain, and loss of sphincter control. In the early stages the symptoms are not diagnostic: weakness of one leg may be thought to be a clinically inapparent poliomyelitis. Pain in the back may be thought to be due to kidney disease or "slipped disk" (although the latter is exceedingly rare in children). Bed or daytime wetting may be considered a reaction against parental authority or against school, or failure to mature. Clumsiness in walking may be considered failure to develop properly, or due to tight shoes, or similar nondescript source. A particularly important sign which can be confusing is "twisted back" or scoliosis. By far the greatest number of scoliotics have improper development of the bones of the spine, but a significant number are associated with spinal cord tumor, to the point at which I believe that

any child with scoliosis has a spinal cord tumor until investigation shows absence of such a mass.

Neurologic examination for spinal cord tumor is difficult—the younger the patient, the more difficult the examination because of the great variation in development of skills in using hands and legs. Early pain is not common, and even when it occurs in the vicinity of the tumor, it may not be associated with obvious neurologic findings. Sensory changes are similarly lacking in early cases. By the time there is paraplegia and definite sensory level the diagnosis may be evident, but irreparable damage may be done. Usually children can cooperate enough to display inequalities in strength between right and left, or between arms and legs. Tendon reflexes are obtainable normally, even in newborn infants, and as with any physical examination, differences between the two sides may be significant. Babinski signs are, or may be, found in infants, but after two years they are probably significant. Early diagnosis may be even more important and more gratifying with spinal cord tumors than with those of the brain, for the operability is much better at earlier stages.

X-rays of the spine are often sufficient to enable one to make a definitely localizing *diagnosis*, for the pedicles may be eroded or widened. Frequently it is valuable and necessary to x-ray the entire spine when there is no definite sensory level, for early cervical spinal cord neoplasms may give symptoms chiefly referable to the lower extremities. When the films are not helpful (in about 50 per cent of cases), spinal puncture and myelography may be undertaken. Again much care is needed in the cerebrospinal fluid study, for Queckenstedt's test for block here may be important. If there is a block (i.e. poor or deficient rise in cerebrospinal fluid pressure on compression of the jugular veins), it may be desirable to add an opaque material at that time, and examine the child under fluoroscopic screen to identify the exact level of block. After such a procedure, which may involve removal of considerable cerebrospinal fluid, a somewhat mobile tumor may be induced to move to compress the spinal cord more than before. Consequently, after spinal puncture or myelography, the neurologic status must be examined repeatedly: if signs progress, immediate laminectomy may be in order.

There are few other diagnostic procedures of value: in rare instances electromyography may be of value in differential diagnosis, especially when cerebrospinal fluid study shows no block and the symptoms are chiefly those of the motor system. Then the records may show signs of isolated nerve root involvement, or changes compatible with primary muscle disease.

In rare instances radiation *therapy* may be undertaken without operation—as when there is as yet no block and only some weakness results from epidural masses of Hodgkin's disease, known perhaps from biopsy

elsewhere. Most of the time, decompression needs to be done, as with sarcomas in the epidural space. Here removal of bone alone usually suffices. If the mass, however, is not present in the region between bone and dura mater, the latter must be opened. If, as sometimes happens, the exact level is not immediately apparent, passage of a rubber catheter intradurally upwards or downwards may quickly locate the mass. If the tumor is outside the spinal cord, as with neurofibroma, it may be completely removable—or at least the spinal portion may be removed, leaving for a later day the intrathoracic attack for the other portion of a dumbbell neurofibroma.

Most difficult to deal with, of course, are the intrinsic tumors—gliomas, teratomas, epidermoids, and the like. The widened spinal cord may be discolored, and indicate the location. Usually it is best to slit the dorsal columns longitudinally, and get at least a biopsy. In some instances an elongated intraspinal mass can be apparently completely removed, and leave a still-functioning spinal cord. This is not the usual state of affairs, however, and the decision as to when to stop is a difficult one. Some of the intraspinal masses turn out to be insensitive to x-ray therapy, but if the histologic nature of the tumor appears to warrant the treatment, it should be given.

Postoperative care of the patient is often prolonged, especially if there is paraplegia. The poor nutrition of such patients is well known, and difficult to combat. All the resources of a number of specialties may be needed—urologist, plastic surgeon, orthopedic surgeon, and especially the child's own doctor to coordinate the special interests.

If the child is able to get about after the operation, questions often arise about the site of the laminectomy. It is sometimes true that kyphosis develops because of interference with normal bone growth, and later orthopedic procedures may be necessary. When the pedicles and articular processes are not involved, however, interference with proper growth is not striking, and the concern then is for safety at the boneless area. Body-contact sports and those in which the back could be struck must be forbidden. When only one or two laminae are missing, scarring may be so dense as to afford almost perfect protection.

Prognosis

The incidence of benign tumors of the spinal cord in children is not high: when such a tumor has been removed, the outlook is good (except such instances as neurofibroma in a child with *café au lait* spots and other stigmata of von Recklinghausen's disease, for new tumors may grow later). For the infiltrative gliomas the prospects are for a considerable survival, albeit with paraplegia and a wheelchair existence. In some patients with thoracic spinal cord tumors careful thought

must be given to deliberate transection and even removal of part of the spinal cord, hoping to save life by blocking the tumor spread. Tumors are about equally distributed between extradural and intradural masses. The former are almost always malignant and cannot be completely removed. The extramedullary intradural tumors (about one-sixth to one-tenth) are usually benign. The intramedullary tumors (about one-third) are usually slow-growing gliomas.

On the whole, the outlook with neoplasms of the central nervous system in children is not a hopeful one at present. Because isolated cures do occur, every attempt must be made to find the tumor and to remove it if possible (if compatible, that is, with proper maintenance of function). There seems little in store in the matter of prevention—more is to be anticipated from the chemotherapy of tumors; may it arrive soon.

SUMMARY

Brain tumors in children are sufficiently common to warrant consideration when one is faced by signs and symptoms which may be caused thereby. These include vomiting of uncertain origin, headache, loss of vision, ocular palsies, unsteady gait, weakness and convulsions. With modern diagnostic techniques, especially with air studies and angiograms, early operation is possible in many cases. Operation may be lifesaving in some instances, and may prolong useful life in others. The mortality statistics are no worse than for cancerous growths outside the nervous system.

Spinal cord tumors in children are much less common than brain tumors. Somewhat over a third are malignant, but others are slow-growing and amenable to palliation. Still others are benign and can be cured. Early diagnosis can be helped by thinking of this possibility when there is complaint of pain in the back, difficulty in walking, weakness, or of scoliosis.

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PROGRESSIVE MUSCULAR DYSTROPHY AND ATROPHY AND RELATED CONDITIONS

Diagnosis and Management

CHESTER A. SWINYARD, M.D.

Although no one of the conditions considered in this clinic could be described as common, nevertheless, collectively, they comprise a large group in which definitive diagnosis is sometimes difficult to make. Many of the conditions are inherited or heritable, and detailed familial data are of great value. In one of the conditions to be discussed (multiple congenital contracture [arthrogryposis]) there is little agreement in the literature whether the primary site of the pathologic process is in the connective tissue, the muscles or the nervous system. In none of the conditions has the etiologic factor been established, nor do we have any pharmacologic agents which will prevent the disease, arrest its development, cure it or significantly alter the natural history of the illness. The prognosis is extremely variable, ranging from a static pathologic lesion with no progression to rapidly progressive disease with death an irrevocable result within 5 to 20 years after onset. For these reasons it is essential that accurate diagnosis be made in order to plan the patient's care and properly to counsel the parents. In spite of an extremely limited pharmacologic armamentarium, comprehensive and effective management can make life much richer for these patients by prevention of deformities and enabling them to achieve maximal functional independence during the progressive stages of the illness. For those who do not encounter these conditions with any regularity, the

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site of the lesion, diagrammatically represented in Figure 50, may be helpful. We shall use the term "progressive muscular dystrophy" with reference to a primary degeneration of striated musculature. In dystrophy the nervous system is intact. Progressive muscular atrophy is a muscular weakness secondary to progressive degeneration of the lower motor neurons of the spinal cord or brain stem from unknown causes (Fig. 50).

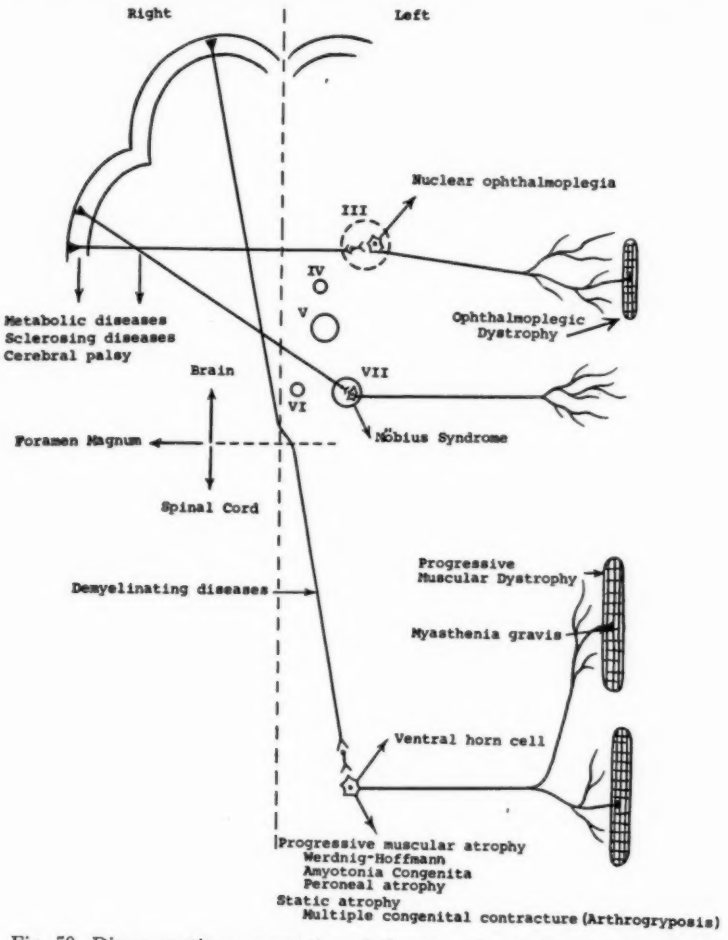

Fig. 50. Diagrammatic representation of the sites of pathologic involvement in syndromes which require consideration in the differential diagnosis of progressive muscular dystrophy.

PROGRESSIVE MUSCULAR DYSTROPHY

General Considerations

It is likely that the appellation "progressive muscular dystrophy" comprises a number of disease entities, characterized by degeneration of striated skeletal and cardiac muscles, of unknown etiology. All the dystrophies have significant hereditary features, and some of the clinical types of dystrophy are accompanied by unusual associated deficits. This, plus the different mechanisms of inheritance and the variation in prognosis in the several clinical types, would tend to support the probability that different biochemical deficits may be responsible for the several clinical types of this illness.

Nutritional Dystrophy

Although it has been nearly 100 years since Duchenne[18] described what is frequently called childhood type of progressive muscular dystrophy, this condition is frequently confused with nutritional muscular dystrophy. In 1928 Evans and Burr[20] made the discovery that laboratory rats deprived of vitamin E underwent degeneration of striated muscles which could be prevented by administration of vitamin E. This led to a wave of hope that human progressive muscular dystrophy is due to such a deficiency. Mason et al.[45] found no deficiency of vitamin E in human patients with progressive muscular dystrophy, and administration of this vitamin has no effect on the degeneration and weakness in human progressive muscular dystrophy. Nevertheless, nutritional (vitamin E) muscular dystrophy has been experimentally produced in more than 20 species of animals, including such diverse species as ducks, lambs[29] and kangaroos.[65] The discovery of a strain of mice which exhibits a hereditary type of dystrophy unrelated to vitamin E deficiency has provided a valuable research animal.[47]

Clinical Classification of Progressive Muscular Dystrophy

There is no general agreement about the clinical classification of dystrophy.[7, 72, 84, 87] None of the classifications proposed have a common denominator from which the several types differ. Perhaps the specific designation of a type is less important than the essential realization of the significant difference which exists between some of the types. We have elected to use the following modification of a classification proposed by Walton and Nattress.[87]

Duchenne (Childhood; Severe Generalized) Type. This is the most common and serious type of progressive muscular dystrophy.[83] It has an onset between ages 2 and 10 years in the muscles of the lower

trunk, hips and lower extremities and gradually progresses cephalically. It is virtually unknown in the female sex. Most patients succumb to respiratory infection or from cardiac failure because the heart muscle becomes involved in the dystrophic process.[22, 93] Death usually occurs before age 20 (Fig. 51).

LIMB-GIRDLE TYPE. This form of dystrophy[87] is intermediate between the Duchenne and the facioscapulohumeral forms with respect to incidence, age at onset and prognosis. It is less severe than the former

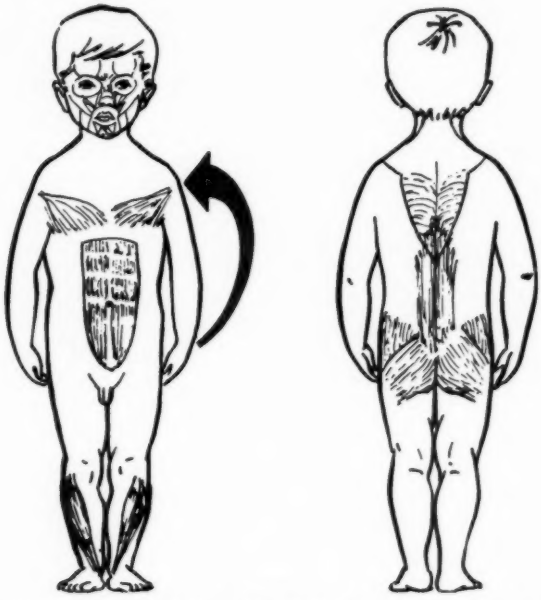

Fig. 51. Diagrammatic representation of the initial muscle involvement and the general pattern of subsequent muscle involvement in Duchenne muscular dystrophy.

and more severe than the latter. It is also more variable than either Duchenne or facioscapulohumeral type. The onset varies between 10 and 40 years of age and may first attack either the pectobrachial or the pelvifemoral muscle groups. The anatomic spread is to the opposite girdle in 2 to 15 years. Hereditary transmission is autosomal recessive without sex linkage (Fig. 52).

FACIOSCAPULOHUMERAL (LANDOUZY-DÉJERINE; MILD RESTRICTIVE) TYPE. This is the third most common clinical type of progressive muscular dystrophy.[82] The onset varies between 10 and 18 years of age. As the name implies, onset is in a particular group of muscles. The disease is equally frequent in both sexes and progresses so slowly that longevity

is not significantly shortened even though severe disability occurs in later life (Fig. 53).

MYOTONIC DYSTROPHY (DISTAL; DYSTROPHIA MYOTONICA). The age at onset is extremely variable. There is no sex predominance, and the distal muscles of the upper extremities are usually first involved. Cortical cataracts, frontal baldness and gonadal atrophy are character-

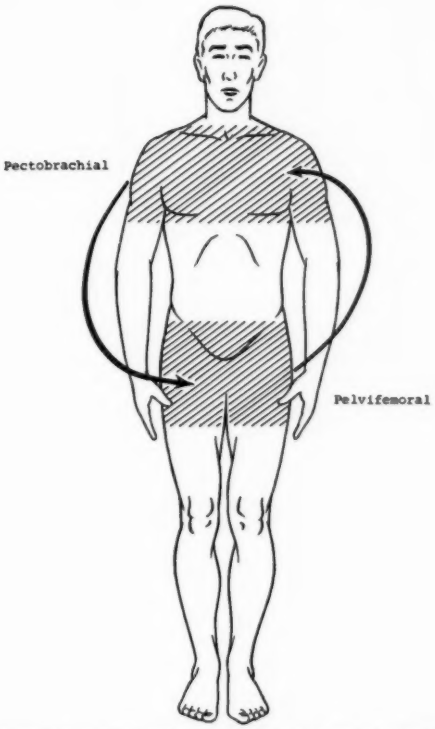

Fig. 52. Diagrammatic representation of the initial muscle involvement and the general pattern of subsequent muscle involvement in limb-girdle type of progressive muscular dystrophy.

istic associated findings.[26] Involvement of the gonads might suggest endocrine imbalance; however, none have been found.[35] The delayed muscle relaxation which occurs after strong voluntary contraction is characteristic of this type of dystrophy. The myotonia may precede or follow the dystrophic degeneration of the muscles. In some cases the myotonia may never occur.[21, 88] For years there has been speculation about the relation between this type of progressive muscular dystrophy and myotonia congenita or Thomsen's disease.[5, 41, 42, 80] Bell[5] believes

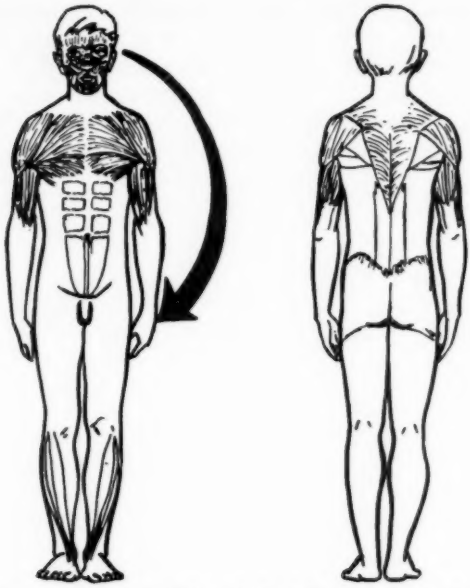

Fig. 53. Diagrammatic representation of the initial muscle involvement and the general pattern of subsequent muscle involvement in facioscapulohumeral progressive muscular dystrophy.

TABLE 25. *Summary of Bell's Criteria for Differentiation of Myotonia Congenita (Thomsen's Disease) from Myotonic Dystrophy*

	MYOTONIA CONGENITA (THOMSEN'S DISEASE)	DYSTROPHIA MYOTONICA
Age at onset	Usually congenital	75% after 15 years
Myotonia	Widespread	Usually over restricted area
Muscular signs	Hypertrophy common	Weakness and wasting in characteristic areas
Cataract	No association	Frequent association
Baldness	Not characteristic	Characteristic
Testicular atrophy	Not characteristic	To be expected
Tendon reflexes	Usually normal	Usually lost early in disease
Mental condition	Associated psychosis	Deterioration common
Genetic basis	Dominant suppression rare	Dominant suppression often demonstrable

that these are separate disease entities; however, Maas,[41, 42] who has had a large experience with both syndromes, considers myotonia congenita (Thomsen's disease) and paramyotonia to be variants of myotonic dystrophy (Fig. 54). The points of difference as to this relation are summarized in Table 25.

OPHTHALMOPLEGIC DYSTROPHY. In this type of dystrophy the muscle

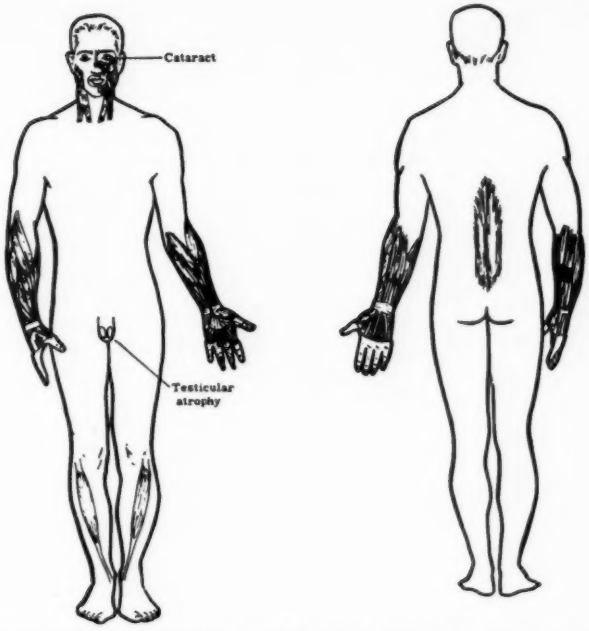

Fig. 54. Diagrammatic representation of the initial muscle involvement and the associated defects in myotonic progressive muscular dystrophy.

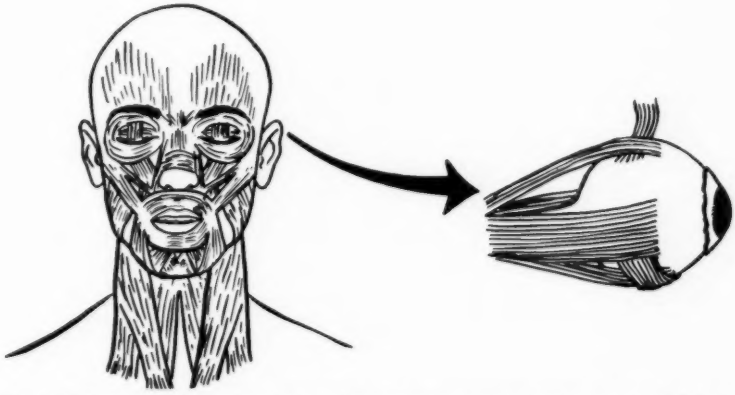

Fig. 55. Diagrammatic representation of the primary muscle involvement in ophthalmoplegic progressive muscular dystrophy.

degeneration is largely confined to the extrinsic muscles of the eyes. It can best be differentiated from nuclear ophthalmoplegia by electromyographic study[39] (Fig. 55).

Hereditary Considerations

All types of human progressive muscular dystrophy are heritable or hereditary.[5, 14, 51, 82, 83] Typical patterns of inheritance of three of the

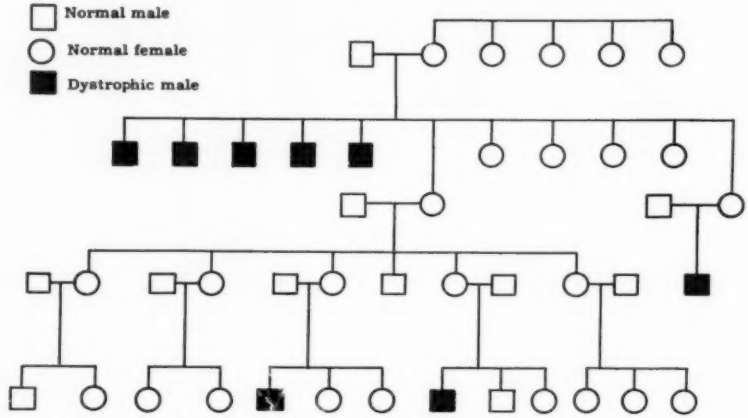

Fig. 56. Pedigree of a kindred exhibiting sex-linked recessive inheritance of Duchenne (pseudohypertrophic) muscular dystrophy. Only males are affected.

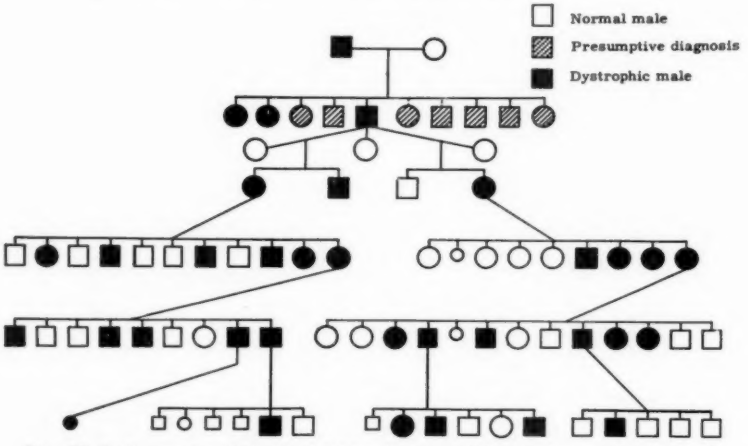

Fig. 57. Pedigree of a kindred exhibiting facioscapulohumeral muscular dystrophy. Note the pattern of dominance without sex linkage. Nineteen dystrophic males and 15 dystrophic females in 6 generations of a kindred comprising 79 individuals.

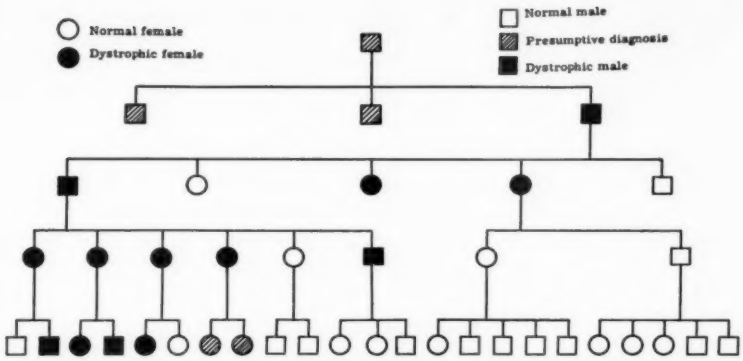

Fig. 58. Pedigree of a kindred exhibiting myotonic dystrophy transmitted as a dominant trait without sex linkage. Eight dystrophic males and 10 dystrophic females in a kindred of 40 individuals comprising 5 generations.

five clinical types are illustrated in Figures 56 to 58. The sex-linked recessive patterns of inheritance in Duchenne dystrophy are of special interest. These patients are so severely incapacitated by adolescence that marriage of an affected person rarely occurs.[51] This type of dystrophy has one of the highest mutation rates known in human genetics (1×10^{-4} Haldane formula) (89 per million gametes[51]).

Incidence

Until recently there were few accurate data as to the incidence of progressive muscular dystrophy; however, from the prognostic viewpoint it is one of the most serious disabling diseases of childhood. Recently Chung[14] and Morton[51] have analyzed the available adequate genetic data and combined these with the data from the University of Wisconsin muscular dystrophy clinic and have computed the incidence, prevalence and mutation ratio for four clinical types of dystrophy (Table 26).

PROGRESSIVE MUSCULAR ATROPHY

This group of diseases is characterized by muscular weakness secondary to deficit in the number of functioning ventral horn cells of the spinal cord and/or the clusters of motor nerve cell bodies in the brain stem (Fig. 50). As in the dystrophies, there is among the atrophies a number of syndromes in none of which is the etiology known. Likewise there is no known method of prevention, arrest or cure of these conditions; in fact, the separate identity of some of the eponymic syndromes is extremely confused.

TABLE 26. *Prevalence, Incidence and Mutation Rate of 3 Clinical Types of Progressive Muscular Dystrophy*

TYPE OF DYSTROPHY	PREVALENCE	INCIDENCE	MUTATION RATE
Duchenne	66 living cases/million males	279 males/million male births	89/million gametes
Limb-girdle:			
autosomal recessive cases	12 living cases/million	38/million births	31/million gametes
sporadic cases	8 living cases/million	27/million births	31/million gametes
Facioscapulohumeral	2 living cases/million	4/million births	5/10 million gametes

Based on computations of Chung and Morton.[14, 51]

WERDNIG-HOFFMANN DISEASE

This syndrome was described[32, 89] as a progressive muscular atrophy whose symptoms do not appear until the latter half of the first year of life. The paralysis rapidly progresses from the trunk to the shoulder and pelvic girdle, then to the proximal limb muscles. Biopsy,[60] autopsy[10] and electrodiagnostic studies[25] clearly indicate this to be a deficit of lower motor neuron function. Most of the patients are said to die before the age of 12 years. It is inherited as a recessive trait or as a dominant with low penetrance.[9, 10]

OPPENHEIM'S DISEASE (AMYOTONIA CONGENITA)

Nearly 10 years after Werdnig[89] and Hoffmann[32] described the previously mentioned syndrome, Oppenheim[53] described 3 cases characterized by universal muscle weakness, hypotonia and hypermobility of joints. Onset of the disease is presumably before birth. Oppenheim emphasized the favorable prognosis; all three patients died, however, after his death, and autopsy study of the three cases revealed extensive lower motor neuron degeneration. Greenfield and Stern[27] concluded that these two syndromes are but variants of a single pathologic process. Brandt[9, 11] studied the prognosis of 112 patients and found that 80 per cent died before the age of 4 years. Walton[85, 87] followed up 109 patients who had been diagnosed as having amyotonia congenita and found that only 8 had complete recovery and that 55 died before their twelfth year. In spite of these data, there is a widespread impression that amyotonia congenita is a relatively benign condition with a good prognosis for recovery. Walton[86] recently extended the concept of amyotonia by creating the following subdivisions: (1) infantile progressive muscular atrophy and related syndromes; (2) symptomatic hypotonia—muscular, cerebral nutritional and metabolic disorders characterized by hypotonia; and (3) benign congenital hypotonia—partial or complete recovery with myopathic electromyographic pattern.

Greenfield and Stern[27] observed diminished numbers of hypoglossal nuclear cells in all necropsy cases they studied. We[79] have seen fibrillation of the tongue in approximately one third of 60 patients we have studied. The delicate, quivering, circus movements of fibrillation must be carefully distinguished from tongue tremor. The question of prognosis and certain diagnostic features of these two eponymic syndromes will be discussed in connection with prognosis.

CHARCOT-MARIE-TOOTH DISEASE (PERONEAL ATROPHY)

The onset of this syndrome may occur any time between 12 and 50 years of age. The initial weakness is usually in the extensor erector

muscles of the foot and results in an equinovarus foot deformity. Occasionally the onset is initially in the distal upper extremities and may be accompanied by paresthesia and sensory loss.[19]

DIAGNOSIS OF PROGRESSIVE MUSCULAR DYSTROPHY AND ATROPHY

When one enters into the diagnosis of progressive muscular dystrophy and its differentiation from a host of conditions with which it may be confused, one lands immediately into the heart of a large variety of the most confused neurologic syndromes and metabolic diseases characterized by muscle weakness that have been described. Reference to Figure 50 will indicate that the primary site of the lesion in these conditions may vary from the cerebral or cerebellar cortex, spinal cord and peripheral nerves, motor end plate or the muscle itself.

We have previously described the principal clinical types of progressive muscular dystrophy and have outlined the important features of the several clinical types of progressive muscular atrophy. It is essential not only that one make the diagnosis of progressive muscular dystrophy, but also that attempts should be made to differentiate the clinical type of progressive muscular dystrophy because of the great variability in prognosis among the clinical types of the disease.

It is first important to know whether the onset of the muscular weakness prevented or occurred after normal muscular development and acquisition of patterns of motor activity at the proper age. Although the occurrence of congenital Duchenne type of progressive muscular dystrophy has been described,[4] it is so rare that a history of normal development of ambulation for about one year or more would tend to implicate a dystrophic process rather than a congenital or infantile progressive muscular atrophy, such as Werdnig-Hoffmann or Oppenheim's disease. A further point of distinction between these two groups is related to the site of initial weakness and the anatomic sequence of muscle involvement. In the several clinical varieties of progressive muscular dystrophy the site of initial weakness and progressive sequence of involvement is indicated in Figures 51 to 55. On the other hand, in the congenital and infantile atrophies the muscle weakness is usually universal.

The pattern of hereditary transmission is so characteristic in the Duchenne type of progressive muscular dystrophy that it offers some diagnostic assistance. For example, occurrence of Duchenne type of progressive muscular dystrophy in a female patient is so rare that this probability can be virtually excluded by reason of the sex. Hereditary cases of the infantile atrophies occur uncommonly and are not sex-linked.

There is considerable difference of opinion as to the relative value of muscle biopsy versus electromyographic study and biochemical study for differentiating between the primary progressive degeneration of striated muscle (progressive muscular dystrophy) and muscular weakness incident to ventral horn cell disease (progressive muscular atrophy).[13, 92] During a study of what was called "The Floppy Infant," Greenfield et al.[28] concluded that biopsy and histologic study were more reliable. This may be so when the biopsy site is carefully selected with considerable knowledge of this group of diseases and the histologic specimens are well prepared. On the other hand, it has been our experience with a high percentage of the patients referred to a muscular dystrophy clinic who have had biopsy study that the report was inconclusive. The specimen was largely connective tissue without enough muscle to determine whether the degeneration was random or on a motor unit basis. The occurrence of rapid low voltage potentials in dystrophy,[66] as compared with the classic electromyographic signs of neurogenic weakness, has been abundantly documented[13] and, in our experience, has been found to be more reliable for differentiation between these two major groups of diseases.

Although it has long been known that in progressive muscular dystrophy there is increased urinary creatine and decreased secretion of creatinine,[49, 66] it is now generally acknowledged that these substances are altered in this manner in almost any disease characterized by muscle wasting and have neither diagnostic nor prognostic value. In recent years attention has been devoted to alterations of concentration of certain enzymes. White and Hess[91] found no alteration of phosphatase activity, but found elevated aldolase and transaminase activity in progressive muscular dystrophy (see also p. 538). Pearson[56] found transaminase activity always elevated in pseudohypertrophy and suggested that the test might be of merit in evaluating therapeutic procedures. On the other hand, Conrad[15] has shown that it has no diagnostic value for progressive muscular dystrophy by finding transaminase elevated in 92 per cent of a series of patients with myocardial infarction and 50 per cent of the patients with acute rheumatic carditis. Ratner[58] found it elevated in hepatic disease and muscle-splitting operations. Increase in aldolase in tumor-bearing animals was described in 1948.[68] Schapira et al.[64] were first to describe alteration of this enzyme in progressive muscular dystrophy. Although Aronson and Volk[3] found aldolase elevation in neurogenic atrophy, Thompson and Vignos[81] found virtually normal values in amyotonia congenita, elevated values in early progressive muscular dystrophy and approximately normal values in late cases of progressive muscular dystrophy. It is of interest that Thompson and Vignos made no effort to classify the dystrophy

TABLE. 27. *Conditions Which Require Consideration with Reference to Insidious Onset of Muscle Weakness*

DISEASE	AGE AT ONSET	INITIAL AREA OF MUSCLE WEAKNESS	PROGNOSIS	ASSOC. DEFECTS OR DIAGNOSTIC POINTS	INHERITANCE	NEUROLOGIC	
						Motor	Sensory and/or Mentation
Progressive muscular dystrophy:							
Duchenne	2–10 yrs.	Glutei, abdom., ant. tibial, erector spinae	Poor, die before 25	EMG rapid, low voltage. Cardiac involvement	Sex-linked recessive	No abnormality	No abnormality
Limb-girdle	10–40 yrs.	Pectobrachial or pelvifemoral groups	Poor, death middle age		Autosomal recessive	No abnormality	No abnormality
Facioscapulohumeral	10–18 yrs.	Shoulder, face, pectoralis maj., low trapezius	Fair, slow progress		Somatic dominant	No abnormality	No abnormality
Myotonic	15–80 yrs.	Hand, forearms, sternocleidomastoid, masseters	Poor	Cataracts, gonadal atrophy, myotonia	Somatic dominant	Myotonic EMG pattern	No abnormality
Ophthalmoplegic	1–40 yrs.	Extrinsic eye muscles	Good—only disabling	Myopathic EMG pattern	Somatic dominant	Myopathic EMG	No abnormality
Progressive muscular atrophy:							
Werdnig-Hoffmann	6–12 mos.	Trunk, shoulder, proximal limb	Poor, 5 years	Neurogenic EMG	Recessive	Lower motor neuron	None
Peroneal muscular atrophy	12–50 yrs.	Extensor, evertor foot muscles	Fair, slow	Neurogenic EMG	Dominant or sex-linked recessive	Lower motor neuron	Peripheral neuropathy sensory deficit common
Amyotonia congenita	Congenital	Universal	Fair, depends on severity	30% tongue fibrillation, neurogenic EMG	Occ. dominant	Lower motor neuron	None
Benign congenital hypotonia: **Walton**	Congenital	Universal	Fair–good	Myopathic EMG		No abnormality	No abnormality
Ataxia:							
Friedreich's	6–15 yrs.	Distal lower extremity	Poor	Pes cavus, scoliosis, nystagmus	Recessive or dominant	Dim. reflexes in low. ext.	Proprioceptive loss, vibratory loss
Marie's	After 20 yrs.		Fair	Involves olive, pons and cerebellum	Dominant or recessive	Hyperactive	
Inflammatory disease of muscle:							
Polymyositis:							
acute	Children	Shoulder and proximal ext.	Poor	Fever and pain frequent		No abnormality	No abnormality
chronic	Adults	Lower extremity, upper	Poor	Skin lesions; muscle tender		No abnormality	No abnormality

End-plate disease:							
Myasthenia gravis	10–70 yrs.	Ocular, facial, deglutition		Tensilon test, EMG		Muscle weakness only	No abnormality
Demyelinating diseases:							
Schilder's disease	Birth–senil.	Neck and extremities	Poor, var. wks.–yrs.		Familial	Spasticity, athetosis, ataxia	Cortical blindness, hearing loss, dementia
Krabbe's disease	4–6 mos.	Dysphagia, then generalized	Poor—death 1 year		Familial	Rigidity/flaccidity	
Multiple sclerosis	15–50 yrs.	Variable	Poor	Paresthesia, diplopia, vertigo	Not of significance	Spasticity variable	Impaired
Amyotrophic lateral sclerosis	20–50 yrs.	Variable	Poor—5 yrs.	Fasciculation	Not hereditary	Upper and lower motor neuron	No abnormality
Metabolic disorders of the nervous system:							
Lipoidoses:							
cerebromacular degeneration (Tay-Sachs)	3–6 mos.	Neck, trunk, extremities; becomes universal	Poor—2–4 yrs.	Prog. blindness, dementia, paralysis, retinal cherry-red spot	Recessive	Flaccidity, spasticity	Retinal blindness
cerebromacular degeneration (Spielmeyer Vogt)	4–18 yrs.	Universal	Slow—10–15 yrs.	Macular brown spot	Dominant or recessive	Flaccidity, spasticity	Retinal blindness
Niemann-Pick disease	Same as Tay-Sachs except for hepatosplenomegaly and skin discoloration. Defect of sphingomyelin metabolism						
Hurler's disease (gargoylism)	Defect of phospholipid metabolism. Impaired vision. Dwarfed. Hepatosplenomegaly. Mental retardation. Generalized weakness						
Gaucher's disease	Defect of keratin metabolism. Hepatosplenomegaly. Rapid paralysis when nervous system is involved. Dysphagia and laryngospasm						
Carbohydrate:							
galactosemia	Absent P Gal transferase activity. Generalized weakness						
glycogen storage disease	Deposit of glycogen in muscles and nerve cells. Generalized weakness						
maple sugar disease	Defective metabolism of valine, leucine and isoleucine. Retarded motor development						
Protein:							
Phenylketonuria	Deficient phenylalanine hydroxalase. Mental retardation. Delayed motor development						
Amino-aciduria	Hypoamino-acidemia and hyperamino-aciduria. Delayed motor development						
Hormonal disorders:							
Thyrotoxic dystrophy	Pectoral and pelvic girdle muscle weakness disappears in euthyroid state						
Menopausal dystrophy	Pectoral and pelvic girdle muscle weakness. Responds to cortisone administration						

patients according to clinical type. Among 50 muscular dystrophy patients whose aldolase levels were studied were 9 females, all of whose enzyme levels were near normal. The females were likely examples of limb-girdle or facioscapulohumeral dystrophy in whom the rate of muscle degeneration is slower than in the male with Duchenne type of dystrophy. Is it, therefore, possible that the near-normal values in amyotonia congenita are an indication that loss of muscle mass is no longer occurring? Perlstein (personal communication) also finds aldolasemia in early Duchenne dystrophy and dehydrogenasemia in facioscapulohumeral dystrophy.

Geiger and Garvin[23] could culture muscle fibers from dystrophy patients through only one passage, and the fibers had a shorter dormancy than normal fibers, which could be subcultured 12 successive times. Perlstein finds tissue culture more reliable than enzyme study, but, among the latter, aldolase levels most reliable for diagnostic purposes.

It is our opinion that, for practical purposes, with due attention to the hereditary features, careful detail with reference to age at onset, initial groups of muscles involved and the anatomic sequence of involvement and electromyographic study, diagnosis and differentiation from the atrophies can be made accurately without resort to either enzyme study or tissue culture. On the other hand, for research purposes, tissue culture, enzyme and other biochemical studies should be done because, undoubtedly, in this area the question of etiology eventually will be answered.

In addition to differentiation of the progressive muscular dystrophies and atrophies, there are many other diverse pathologic conditions characterized by muscle weakness. The conditions range from congenitally occurring weakness to onset in adult life. Limitations of space preclude discussing them in detail, but a number of the pathologic entities which must be remembered in this connection are listed in Table 27. The abbreviated list of conditions is only suggestive of some areas which need to be recalled in connection with the onset of muscle weakness whose etiology is not readily apparent. In general, when the diagnosis of progressive muscular dystrophy or atrophy in children is in doubt, attention should be directed to the metabolic disturbances of lipids, phenylalanine or other amino acids, carbohydrates or mental retardation. Laboratory tests for urinary phenylpyruvic acid,[6] serum galactose and amino-aciduria are not difficult. Onset of initial muscle weakness in adults which appears not to be either dystrophy or lower or upper motor neuron disease, or a combination of the latter two, should cause one to think of menopausal[69] or thyrotoxic dystrophy,[50] alcoholic or other types of polyneuritis, diabetic or interstitial neuropathy, disuse atrophy from pain or a psychoneurotic syndrome.

CONSIDERATIONS OF PROGNOSIS

Comprehensive management of either progressive muscular dystrophy or atrophy must take into consideration prognosis. We have previously indicated that, among the dystrophies, prognosis may range from a likely possibility of death by the end of the second decade of life in Duchenne dystrophy to little or no diminished longevity in facioscapulohumeral dystrophy. With reference to the congenital or infantile atrophies (Oppenheim's and Werdnig-Hoffmann disease), if one accepts the evidence which indicates the identical nature of these syndromes, then one must consider the prognosis of the so-called amyotonia congenita to reflect the dismal picture usually conceded for Werdnig-Hoffmann disease.

Presently we see at periodic intervals approximately 40 patients with the clinical diagnosis of amyotonia congenita. The ages of these patients range from 2 to 34 years. The electromyographic findings are similar to those previously reported in Werdnig-Hoffmann disease.[13] A number of these patients have had repeated electromyographic study without evidence of change. Muscle power has not changed in 10 years in the older patients; nevertheless, the younger children frequently lose functional motor ability between age 2 and 4 years. We believe that the following considerations are worthy of reflection in this connection.

Is it possible that, at one year of age, with a marginal number of motor units available in a muscle to move a given part weighing 1 pound, the same marginal group of motor units cannot move the part concerned when, through growth and development, that anatomic part weighs 2 pounds? Also, many of these patients initially have a vital capacity which is 30 per cent of normal. As scoliosis develops, vital capacity diminishes, lung noncompliance increases, and the ability of the patient to withstand upper respiratory tract infections diminishes. Finally, all previous data on prognosis in the childhood atrophies include only children who were born either in preantibiotic or early days of limited use of modern antibiotic therapy. The writer does not have answers to these questions, but suspects that some of these considerations have given a degree of bias to our concept of neurologic progression in the congenital and infantile progressive muscular atrophies.

RELATED SYNDROMES

MULTIPLE CONGENITAL CONTRACTURES (ARTHROGRYPOSIS)

Although this supposedly rare syndrome of unknown etiology is best known in this country by the term "arthrogryposis," created in 1923 by Stern,[71] it was described by Otto[54] in 1841, and as many as 500 cases

have been described in the world's literature under a great variety of names.[16, 33, 44, 48, 52, 54, 61, 63, 67, 71]

There has been much speculation about the etiology of this condition. Some have been impressed by the thickening of the joint capsules of the contracted joints and have believed it to be a connective tissue disease.[43, 70] Others have had their attention drawn to the lack of de-

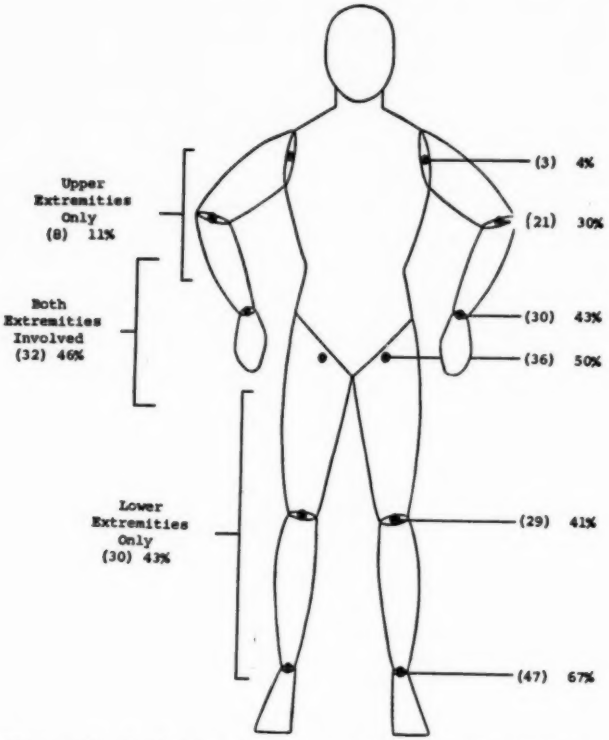

Fig. 59. Topographic distribution of involvement in 70 cases of multiple congenital contractures.

velopment of striated muscle and have postulated myoblastic failure of development.[67] The final group comprises those who have presented evidence for neurogenic origin of the disease, based on autopsy findings[8, 24, 38] and electromyographic study.[76] Almost every conceivable combination of flexion or extension contracture in various combinations has been described. The distribution of the contractures we[77] found in 70 cases is illustrated in Figure 59. This condition is generally said not to be hereditary;[36, 46] however, we have described three kindred

exhibiting hereditary cases,[74] in one of which there were eight cases in three generations of the family which exhibited autosomal dominant transmission.

This syndrome has been considered rare; however, we have pointed out that, when one considers the cases reported under its multiple synonyms, those unrecognized and described as some other condition,[8, 57] and association of this condition with the Moebius syndrome[37] and arachnodactyly,[40] it is much more common than is generally realized.[77]

In our study we[77] found a significant number of these patients born with other serious anomalies which are incompatible with life. We have estimated that there may be as many as 500 new occurrences of this syndrome annually in the United States. This brief review of this poorly understood syndrome is motivated by its likely relation to the congenital muscular atrophies. Brandt[8] and the writer[74] have observed monozygotic twins in whom one member of the pair presented the clinical state of amyotonia congenita and the other multiple congenital contractures. Several autopsy reports[8, 24, 57] have described loss of anterior horn cells in the spinal cord. Joseph et al.[37] studied one patient electromyographically, and Lefebvre and Chaumont[40] studied three cases; both reported evidence of neurogenic atrophy. We[76] have studied 10 cases electromyographically, and in most instances the findings were similar to those reported for amyotonia congenita or Werdnig-Hoffmann disease.

We believe that these data suggest that, in a significant percentage of instances, the syndrome of arthrogryposis is but a variant of the Oppenheim-Werdnig-Hoffmann infantile muscular atrophies. It is conceivable that there is great variation among these atrophies from the viewpoint of the proportion of motor cells involved as well as onset earlier or later in intrauterine life. If the same mechanical factors which cause contracture postnatally are operative in utero, could it not be that intrauterine contracture could likewise be produced? Because of this possibility of relation to the congenital atrophies, we have briefly mentioned this syndrome, even though diagnosis of the condition is made obvious by birth with multiple congenital contractures.

MOEBIUS'S SYNDROME (CONGENITAL FACIAL DIPLEGIA)

This condition is a congenital facial diplegia of nuclear origin. Frequently, nuclei of the abducens, hypoglossal and oculomotor nerves are also affected. Autopsy[34] and electromyographic studies clearly indicate this to be a lower motor neuron disease. A review of the literature would indicate that nearly one third of the cases which are generally described in the ophthalmologic literature have multiple con-

genital contractures of the extremities.[30] Likewise, we have seen cases of arthrogryposis that had the congenital facial diplegia and cases described in the orthopedic surgery literature which mention eye and face paralyses without mention of the eponymic connotation.

MARFAN'S SYNDROME (ARACHNODACTYLY)

This syndrome is characterized by long, thin bones of the extremities, subluxation of the eye lens, and cardiovascular and other anomalies. Several of our cases of multiple congenital contractures have been associated with this syndrome, and this association has been discussed in the literature.[59] The ophthalmologic literature, which details the lens subluxation, also gives case reports which mention associated multiple congenital contractures without associating this phenomenon with arthrogryposis.

We do not intend to imply by brief mention of these three syndromes that they are all variants of the same process, but these associations do give some circumstantial support to the postulation that a large percentage of the cases of arthrogryposis are neurogenic in origin and may be related to the infantile atrophies of Oppenheim-Werdnig-Hoffmann. Perhaps the associated anomalies are reflections of the effect in different fetal tissues of a single causative agent at a vital time in embryonic or fetal life.

MANAGEMENT OF THESE CONDITIONS

Reflection about the diversity of possible etiology, prognosis and patterns of hereditary expression makes it apparent that space limitations restrict one to general principles and areas of treatment rather than specifics.

At the outset we must reiterate that there is not yet available a pharmacologic compound of any proved value in prevention, arrest or cure of the conditions considered here.

We have felt keenly the need to view the natural history of these conditions in longitudinal perspective because it enables us more rationally to plan a rehabilitation program. We[78] therefore devised a functional grading system of the progressive changes in the patient's ability and method of ambulation (Table 28). If one uses these gradients of functional ability and plots on a grid the stage of activity reached at a given age, one can more easily visualize the natural history of these conditions. In Figure 60 such a grid illustrates the changes in a typical case of Duchenne dystrophy, facioscapulohumeral dystrophy and amyotonia congenita.

TABLE 28. *Criteria for Identification of 8 Stages of Functional Ability*

1. Ambulates with mild waddling gait and lordosis. Elevation activities adequate (climbs stairs and curbs without assistance).
2. Ambulates with moderate waddling gait and lordosis. Elevation activities deficient (needs support for curbs and stairs).
3. Ambulates with moderately severe waddling gait and lordosis. Cannot negotiate curbs or stairs, but can achieve erect posture from standard-height chair.
4. Ambulates with severe waddling gait and lordosis. Unable to rise from a standard-height chair.
5. Wheelchair independence: Good posture in the chair; can perform all activities of daily living from chair.
6. Wheelchair with dependence. Can roll chair, but needs assistance in bed and wheelchair activities.
7. Wheelchair with dependence and back support: Can roll the chair only a short distance, needs back support for good chair position.
8. Bed patient: Can do no activities of daily living without maximum assistance.

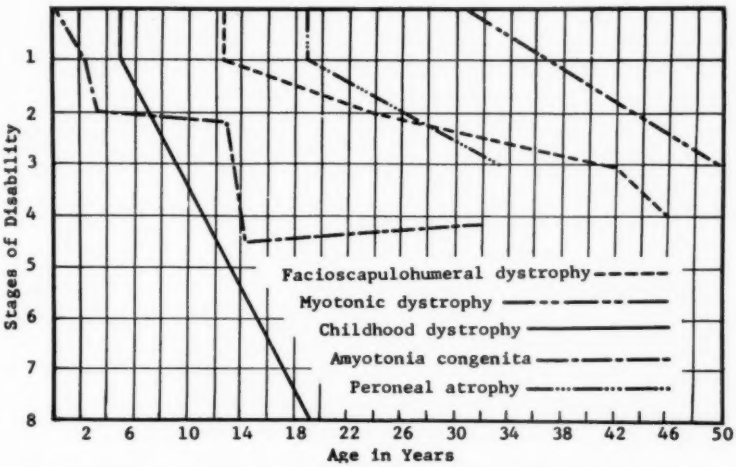

Fig. 60. Changes in functional ability as related to age in patients with Duchenne, facioscapulohumeral and myotonic progressive muscular dystrophy and infantile (amyotonia congenita—Oppenheim) and adult (peroneal atrophy) progressive muscular atrophy.

The philosophy of management is to maintain a maximal level of physical efficiency and independence during the changing phases of the disability. One must also be alert to the factors in the psychosocial aspects of the child's illness which create in the patient or the parents attitudes which interfere with satisfactory psychological adjustment of those involved. Although authors have described the "devastating emotions" found in patients with muscular dystrophy,[90] we have called attention to the possibility of projecting one's own value system into the interpretation of the emotional factors in progressive muscular dys-

trophy.[73] Nevertheless, continual alertness to the social and emotional factors is a keystone to motivation of the patient and understanding of the parent without which a physical activity program, devoted to maximal physical efficiency and prevention of deformity, will probably fail.

Physical Therapy

There is a common tendency among parents of these children to feel that, if their child could have adequate physical therapy for a sufficient time, great improvement would occur. It is our experience that while a patient is in the ambulatory stage, the very act of ambulation can well provide all the needed physical therapy. Abramson[1] found that physical therapy provided some improvement in muscle strength, but this may have been elimination of disuse atrophy. In a controlled study Hoberman[31] found that physical therapy produced no increase in muscle strength, although increased skill in performance of activities of daily living was achieved. Physical therapy would be of value to prevent disuse atrophy in wheelchair patients, and daily range of motion at all joints is essential if deforming contractures are to be avoided. By prevention of contractures and disuse atrophy it is possible to delay the wheelchair stage significantly.

Use of Assistive Mechanical Devices

Braces. It must be remembered that, in order to support the body at a given joint, the brace must cross that joint. For example, if the weakness extends to the trunk and abdominal muscles, the brace must be extended to the chest with a Knight spinal attachment and abdominal support attached to the pelvic band of the brace. On the other hand, if, in an early case, the problem of ambulation is complicated with an unstable foot position, a short leg brace with a 90-degree posterior stop may be all that is required for a number of years. As the weakness progresses, more bracing will be required. If there is insufficient muscle power for ambulation without braces, it will not be possible to ambulate with braces. Braces are useful, however, for the physiologic and psychological value of daily standing and prevention of contractures. In many patients trunk bracing provides a much better body alignment and better position for functional use of a wheelchair. The variety of braces, crutches and wheelchairs and indications for the use of the various types are available in the literature.[17, 62]

Wheelchairs. There is a variety of types of wheelchairs[17, 62] and specific indications for use of the several types. It will suffice to emphasize that, with an appropriate functional activity program and prevention of contracture deformities, wheelchair use can be delayed. In too many

of these patients inattention to these details entails premature wheelchair use. A child with Duchenne type of dystrophy may require a wheelchair by the age of twelve. On the other hand, a patient with facioscapulohumeral dystrophy may not require one until sixty years of age.

COMPLICATIONS OF COMPREHENSIVE MANAGEMENT

Contractures

These deformities can, to a large extent, be prevented if an adequate functional activity program is initiated at the proper time. Paul[55] and Archibald[2] have emphasized active exercises, stretching, braces and passive range of motion for preventing and reducing contractures. If these measures fail, plaster wedge casting or surgical measures may be essential.

Infections

As the progressive muscular degeneration involves the muscles of respiration, there is progressive loss of vital capacity. In the infantile atrophies the universal weakness may, at the onset, result in a vital capacity only 25 to 50 per cent of normal. If scoliosis develops, the vital capacity is further reduced and creates greater difficulty in managing intercurrent infections. Prompt and vigorous therapy of upper respiratory tract infections is warranted. Postural drainage and portable chest respirators are useful, but prolonged use of mechanical respirator equipment should be avoided to prevent disuse atrophy. In patients severely involved and prone to recurrent infection, preventive periodic administration of an antibiotic might be considered.

Cardiac Involvement

There is no clinical or pathologic evidence that the primary disease process affects the heart in progressive muscular atrophy. In Duchenne type dystrophy the heart is frequently affected,[93] and failure may occur abruptly. There are inadequate data as to the heart involvement in some of the clinical types of progressive muscular dystrophy.

Obesity

Frequently children whose physical activity is severely restricted have a caloric intake much in excess of their needs. There may be psychological and emotional factors also operative in this regard. In the presence of

marginal functional muscular ability the overweight may seriously interfere with ambulation and functional independence.

THE ROLE OF SURGERY IN MANAGEMENT

Progressive Muscular Dystrophy

In general, extensive surgical procedures which involve prolonged immobilization should be avoided if possible. The decision as to operation should take into consideration the progressive nature of the illness. In this connection it is important to be specific about the clinical type of dystrophy. For example, if one is concerned with Duchenne dystrophy which is progressing rapidly, one would scarcely be justified in doing an ankle stabilization procedure if, in a relatively short time, full control braces are going to be needed for standing purposes.

Progressive Muscular Atrophy

In many cases of progressive muscular atrophy the weakness is so profound that the immobilization disuse, incident to operation, is extremely difficult to overcome. We have seen a number of instances wherein ambulation was possible with crutches before operation, but could not be effected after immobilization. This was the case in the patient whose activity status is plotted in Figure 60.

Arthrogryposis

In this condition, in which the contractures have been established prenatally, manual stretching is rarely effective. In our study of the surgical procedures used in 70 cases of this syndrome,[77] nonsurgical procedures, such as plaster wedging or bracing, or active manipulations, such as closed reduction of hip and knee deformities, were initially used and were started in infancy. If these procedures were ineffective, soft tissue releases, such as medial stripping of the foot, capsulotomies and tendon lengthening, were done. Ankle and tarsal fusions were occasionally used, and in some instances tibial or femoral osteotomies were required. When the hip was involved, the Soutter procedure was generally used. The most radical procedure used was an amputation performed above the elbow on one of our patients. The patient was functionally more efficient and, psychologically, well adjusted to the prosthesis. These examples indicate that, in this static disease with the problem of contractures, surgical procedures are highly individualized. The effective procedures required may extend through the gamut of available orthopedic techniques.

PARENTAL EDUCATION AND COUNSELLING

In order to make effective any comprehensive plan of management, there must be a continuous program of parental education. Unless the parents have a rational attitude toward the problem, anxieties are transmitted to the children and motivation and psychological adjustment disturbed.

Parents with children having one of these diseases are particularly concerned about the hereditary aspects of the disease and have questions about the chances of having another affected child. It is apparent that the advice given might differ if the condition is that of rapidly progressing Duchenne dystrophy, as contrasted with the milder, slower-progressing facioscapulohumeral dystrophy. This is another reason why it is essential that the clinical type of the illness be accurately identified.

We have not found it wise to compute and quote so-called risk figures in response to these questions.[75] We have preferred to suggest that they consider the degree to which this familial condition has interfered with the family interpersonal and social life and their acceptance by friends and the community. They are urged to weigh these debits against the assets of a more complete personal life and thus arrive at a decision of having more children or entering into marriage with or without children. If they are provided with sound heredity data and proper understanding of the illness, most persons will likely follow an appropriate course of action. Whatever course they follow, they will do so with an understanding which will help them in accepting and providing appropriate care to their children in the event that a defective gene is passed to one of their children.

SUMMARY

Progressive muscular dystrophy is a progressive degeneration of striated muscle of unknown etiology. The several clinical types in order of incidence are Duchenne, limb-girdle, facioscapulohumeral and myotonic. These types differ in the mechanism of hereditary transmission, age at onset, initial muscle group involved, sequence of progression and prognosis.

The progressive muscular atrophies result in progressive muscular weakness secondary to loss of ventral horn cells or motor cranial nerve cells. The congenital form (amyotonia congenita-Oppenheim) and infantile form (Werdnig-Hoffmann) are probably variants of the same disease. Evidence is presented that many of these patients appear to have a static neurologic state, but may succumb to intercurrent infection, which is resisted with less success as deformities contribute to lowered vital capacity.

The syndrome of multiple congenital contractures (arthrogryposis) is discussed because of evidence provided by electromyographic study that a number of these cases are of neurogenic origin, presumably from muscle imbalance of the fetal extremity with resultant intrauterine contracture. Circumstantial support to this view is provided by the frequent association of multiple congenital contractures in the well established neurogenic syndrome of congenital facial diplegia (Moebius's syndrome).

In none of the conditions described is the etiology known. Neither is there any known drug which will prevent, arrest or in any way alter the natural history of the disease.

Management of these conditions must take cognizance of the different prognoses in these conditions. The natural history of the conditions can be clearly viewed by plotting the gradients of functional ability with the age of the patient.

The greatest contribution that physical therapy can make is to keep the muscles at maximal efficiency by preventing disuse atrophy and contractures. The period of ambulation can be prolonged by combination of a functional activity program assisted with braces.

Surgical procedures in muscular dystrophy and atrophy must be highly individualized with consideration to the prognosis and avoidance of prolonged immobilization. On the other hand, a great variety of nonsurgical and surgical procedures are frequently necessary to achieve a degree of functional independence in patients with multiple congenital contractures (arthrogryposis). The goal of management is to keep the patient at maximal physical efficiency and independence in activities of daily living. Achievement of this goal is intimately related to an adequate psychosocial program and effective parental education and counselling.

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CHILDREN WITH COMMUNICATIVE DISORDERS

Evaluation and Management

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The speech pathologist sees many children whose difficulties with oral language arise from fairly isolated problems, such as malocclusion, hearing loss or an insufficient soft palate. With such patients he feels fairly secure in initiating training appropriate to these deficits, dental, medical or surgical treatment either preceding the therapy or being done concurrently. When children have neurologic damage, however, he is much more apt to find disturbances in all or many aspects of communicative behavior. Consequently he must consider the whole communication process, including reception, interpretation, formulation of ideas and the projection of them. In addition to oral language, he explores and exploits all other modalities for receiving and expressing thoughts.

Some of the questions basic to his evaluation and training program are (1) Is the level of communicative behavior appropriate for a child's age, his apparent potential and his learning opportunities? (2) If communicative behavior is not what would be expected, how does it differ? (3) Are there clues to possible causes for the deviations? (4) Are there things that might be done to improve communicative skills? Answers are sought by observing the child, taking a careful history of present and earlier status, and administering tests.

A developmental reference system is often used in getting and reporting clinical information because frequently the person having a problem is behaving as a normal person would at an earlier age in his total communicative behavior or in some aspect of it, as attending to

speech or selecting appropriate words for ideas. The development of communicative skills has received a considerable amount of research effort, and although there are many gaps in the information, it does appear that in all aspects the emergence of these skills follows a pattern. Within reasonable limits of error due to individual variation it is possible to say that in any part of language activity a person is performing like a normal person of a particular age.

In making a systematic evaluation or in planning training it is useful to have in mind a possible sequence of neurophysiologic behavior which might be presumed to support language activity. The use of the word "presumed" is deliberate. Certainly one cannot claim to know exactly how the human organism functions in language, but present information and clinical experience do permit formulation of a defensible, though certainly not infallible, construct. A detailed outline might include (1) end-organ sensitivity, (2) reception of sensory information in the central nervous system, (3) analysis and interpretation of sensory information, (4) conceptual activity, (5) formulation of ideas appropriate for expression, (6) selecting appropriate symbols for the expression of ideas, (7) selection of motor patterns for overt expressive behavior, and (8) executing the motor patterns.

The stages suggested above probably represent a continuum rather than discrete units. In the examination any response to a test procedure will invariably involve several phases and not one alone. As an example, a child's response to speech is used to determine hearing acuity. Even though the understanding of quiet voice demonstrates sensitivity to sound, understanding of language and many other factors are involved. A variety of tests will, however, enable the clinician to sort out the different components. Because of the impracticality of attempting isolated tests of discrete aspects of communicative behavior, an outline with more general groupings is followed in the evaluations. They include reception, concept formation, expression, and motor functioning. The examination procedures explained below follow that outline. In the interpretation of the results, however, the more detailed outline is considered.

EVALUATION OF COMMUNICATIVE BEHAVIOR

Assessment of Expressive Behavior

Although it is convenient to discuss the neurophysiology of communication as an orderly series of events proceeding sequentially from end-organ sensation through integrative and conceptual processs to motor production of speech, it is impractical to test the integrity of function at each of these levels in that order. Speech is the end product of language behavior, and the adequacy of a child's speech or oral language

usage is the best single indication of the degree to which there is integrated functioning at all levels of the language process. Therefore the first part of the speech and hearing examination is devoted to observing and analyzing the speech and how it is used. The other aspects are evaluated selectively as indicated by the oral language demonstrated.

The opinion is sometimes expressed that little is to be gained from a speech and hearing examination until a child reaches the age when he should be talking. Although it is true that a child's ability to produce speech sounds accurately can be measured most easily when he begins using these sounds in words, speech and language learning begins in early infancy and follows an orderly and predictable sequence of development. There are measurable stages in an infant's preverbal development which seem to be necessary precursors to normal oral language production. In many children with central nervous system damage, delayed or disturbed development of preverbal vocalization is the earliest sign that special help may be required for them to learn adequate communication skills.

In the first and second months of life most infants produce a few vowel and consonant sounds in noncrying vocalization as part of the gross bodily responses to handling and feeding. In the third and fourth months this vegetative or involuntary vocalization increases, and becomes associated with particular stimuli, such as the sight of the bottle at feeding time. The same vowel sound may be repeated several times in succession, and the infant may coo or laugh as he examines his hand or plays with his rattle. By the sixth month or shortly thereafter most infants go through a stage of vocal development called differentiated babbling. There is increased activity of the lips, tongue and soft palate, resulting in the appearance of new consonant sounds produced in combination with vowels. To the parents the infant has begun to make syllables in place of simple vowel sounds. From seven to nine months the amount and complexity of vocalization increase, and babbling becomes firmly established as voluntary vocal behavior. By 10 months most infants can imitate simple noises or syllables produced by the parents, and by 12 months their expressive vocabulary may consist of 2 to 4 meaningful words.

Normal infants vary to a certain extent in the rate of vocal development during the first year, but infants with neurologic damage who subsequently are found to have communication handicaps are often grossly disturbed or delayed in preverbal vocal behavior. Case histories of infants with prenatal or paranatal central nervous system damage show that noncrying vocal activity is reduced, and in many cases is absent during the first six months. Infants with profound hearing loss may also show a reduction in the amount and complexity of preverbal vocalization, but this may not be noticed until after six months of age, when the

hearing child begins to achieve voluntary control of the lips, tongue and larynx, and to experiment with sound production. Infants with weakness in the muscles of the lips and tongue may show an increase in the amount of vocalization toward the end of their first year or later, but often fail to develop a variety of vocal sounds, and persist in the production of a few vowels or grunts long after others their age are engaging in complex vocal play. When neurologic damage has resulted in intellectual retardation, in the absence of associated sensory or motor deficits, an infant can be expected to develop vocal usage at a rate commensurate with or slightly below his mental age. A notable exception to this rule is the infant or young child with internal hydrocephalus, whose vocal behavior may be accelerated in relation to his motor and conceptual maturation.

In the second year of life a child's oral language develops at a remarkable rate. At 18 months vocal output is still mostly jargon, with an expressive vocabulary of 10 to 20 words, but by 2 years a child has learned from 200 to 300 meaningful words, and is beginning to combine words into simple two- and three-word phrases or sentences. Before this age he may have expressed most of his needs through pointing or gesturing, supplemented by word approximations; but from two years on, oral language is his principal means of communication. By 3 years of age children are using past and present verb tenses and plural nouns correctly, are beginning to use a few adjectives, adverbs, prepositions and conjunctions, and have a speaking vocabulary of nearly 1000 words. At 4 years of age the speaking vocabulary is approximately 1500 words, and sentence structure and grammar are more often correct than incorrect. Most children of this age retell simple stories, and can be depended upon to give reasonably accurate accounts of past and future events.

In recent years normative data have been gathered which permit comparison of a child's level of oral language usage with that expected at his chronological age. Such scales are useful as quantitative measures of oral language development, but are not sufficient for the clinical description of a child's total expressive abilities. With children who do not talk, or whose speech is so impaired that it is not a reliable method of communication, it is necessary to evaluate all the means by which their ideas or needs are expressed. Many children with severe hearing losses, predominantly expressive language disorders, dysarthrias or verbal apraxias may develop efficient use of pointing or gesturing to take the place of speech, and an examination of the complexity of the gesture system may provide a clue to the level of conceptual development. Simple pointing to objects is a relatively low level of manual communication, and in children with good conceptual functioning pointing will be replaced by manual signs or symbols, arbitrary movements which

are used to represent objects or actions. By the age of three to four years children who have no other means of expression may even develop manual sentences made up of a series of these movements.

Children with severe motor involvement of the upper extremities may even be blocked from developing meaningful hand and arm motions, but some will learn to communicate to a limited extent through eye movements and facial expressions. If a child can do no more than signal "yes" and "no" by facial expression or eye movement, he has a potential method for communicating his basic needs, and a way of demonstrating how much he comprehends and retains. In such children careful questioning can provide an estimate of the extent to which expressive behavior is being blocked by motor dysfunction.

If a child does make an attempt to talk, the structure and content of his oral language may indicate specific language functions which are disturbed. A child with a moderate hearing loss or with moderate sensory or motor impairment of the oral musculature should use oral language fairly well, but have difficulty pronouncing words clearly. When auditory acuity is intact, but auditory perceptual or associative processes are disturbed, oral language may not consist of actual words, but may be jargon or random syllable sequences, perhaps normally inflected, and containing an occasional meaningful word. If the difficulty affects word recall or language formulation, the child may be unable to name even the most common everyday objects, or he may speak in a telegraphic style, almost always in the present tense, with frequent reversals of word order and omission of articles, adjectives, prepositions and conjunctions. The child with this type of problem is often difficult to distinguish from one whose word naming and language formulation skills are good, but who cannot select appropriate motor patterns for the expression of concepts. This latter type of disorder, which is sometimes called verbal apraxia, is also difficult to distinguish from a dysarthria or paralysis of the speech musculature. The distinction is important, however, from the standpoint of speech training.

Many of the symptoms associated with speech and language disorders are considered normal expressive behavior at some stage in a child's development. Faulty articulation of some speech sounds is characteristic of all young children, but sounds are learned in an orderly sequence, so that articulatory errors in the speech of a five-year-old might be considered normal production of these sounds for a child of three. Jargon is more characteristic of the 16-month-old than is articulate speech, but is atypical in a child of three. Pointing and gesturing are primary means of communication before 18 months, but decline rapidly after 2 years.

It should be apparent, then, that in evaluating the level of expressive behavior in an infant or young child the significance of any performance

is relative to chronological age, physical and mental development, social environment and emotional adjustment. When the first stage of the evaluation indicates that oral language usage is within normal limits, it is not necessary to go further. If the expressive behavior is noticeably different, many clues are furnished to direct the emphasis of subsequent testing procedures. In summarizing the first step the clinician can make an estimate of the age level reached in the various facets of overt expressive behavior. The remainder of the examination is devoted to studying factors which might be interfering with oral language.

Assessment of Receptive Behavior

In order to understand spoken language, it is not enough that a child have normal hearing acuity. In addition to adequate cochlear sensitivity and unimpaired transmission of nerve impulses from the peripheral receptors to midbrain and cortical levels, there must be association of sensation with previous experiences to form percepts, and integration and elaboration of percepts into concepts. In children with neurologic damage the reception of spoken language can be disturbed or impaired by interruption of function at any of these levels.

For children of six years or older, and for some mature children of four or five, objective test batteries have been devised which measure many aspects of auditory behavior. Sensitivity to pure tones of different frequencies is measured by air- and bone-conduction audiometry. Standardized tests of speech discrimination indicate a child's ability to understand speech with amplification and under difficult listening conditions. In recent years specialized audiological procedures have been developed for adults which test the integrity of the auditory pathways at cochlear, retrocochlear, midbrain and cortical levels. These techniques can be used with some children of 10 to 12 years. In addition, various procedures are available to assess ability to comprehend and retain spoken language. When used by an experienced diagnostician, these and other procedures can yield much information about hearing acuity, auditory perception and receptive language functioning in older children.

At present there is no corresponding series of tests for investigating auditory functioning in infants and very young children with neurologic damage. Recent improvements in techniques of auditory conditioning to electric shock have proved useful in measuring pure tone thresholds with some children, but as yet too little is known about auditory conditioning in infants and brain-injured children to permit their unequivocal interpretation. Some degree of hearing acuity can be inferred from the occipital alpha activity following auditory stim-

ulation during a sleep electroencephalogram, but at present this technique has not been developed for routine clinical use.

In the clinical examination of infants and young children, observation of responses to environmental noise and voice provides a basis for tentative judgments of hearing acuity and use of hearing. Auditory behavior develops in an orderly sequence just as motor behavior does, and the presence or absence of characteristic responses to sound provides an early indication of the extent to which audition may be disturbed. During the first month, for example, sudden loud noises may evoke a gross startle response, indicating that there is some end-organ sensitivity and integrity of auditory pathways at least to the midbrain level. In very hypotonic infants the startle may not be visible, but can be felt if the noise is presented while the infant is being held. In older infants and children the same stimulus may not produce a total bodily reaction, but can be seen as an eye-blink.

Momentary cessation of bodily activity is a characteristic response to sustained sounds of moderate intensity, and even as early as two months of age an infant may seem to "listen" to such a sound or to voice. By four months, and often earlier, an infant will turn his head in the direction of a familiar voice or sound, and older infants will attempt to locate the source of any unexpected sound. Even when the neck flexors are too weak to rotate the head, the localization response may be detected in eye movements.

An infant of six months will usually stop vocalizing momentarily if an adult imitates his vocalization in a quiet voice, and in so doing gives an indication of his level of awareness for voice. Between six and eight months an infant pays more attention to words spoken by his parents, and by nine months he will smile or look around when he hears his own name. The infant of 10 months will imitate syllables spoken by his parents, and by 12 months he understands a few words and simple questions.

The auditory responses which may be elicited in the first few months after birth are reflexes which seem to be mediated at or below the midbrain, so that their presence indicates only that there is some central reception of auditory sensation. Peripheral deafness may be suspected if an infant consistently fails to demonstrate these responses, but their presence does not indicate the degree to which the infant ultimately will be able to utilize his hearing. The auditory responses observed in the second six months of life depend increasingly upon the development of perceptual and conceptual processes, i.e. the ability to listen selectively, to assign meaning to auditory sensation, and to associate auditory percepts.

From one year on auditory behavior develops through further refinement of auditory perceptual skills and elaboration of percepts and

concepts. This is seen in the child's increasing ability to understand spoken language. Most children of 15 to 16 months can point to simple pictures in a familiar book. By 18 months they can point to their eyes, ears or mouths, and will look for the mother or father when asked where they are. By two years they will sit for a few minutes and pay attention while pictures are named, and at three years they will listen to simple stories such as "The Three Bears."

Assessment of hearing acuity and use of hearing is often the most difficult part of the examination of a young child with neurologic damage. A normal child is inconsistent in his responses to environmental sounds and speech, and the child with central nervous system damage shows even greater inconsistency. Auditory perception seems to develop slowly in many of these children, so that they may be delayed in developing listening behavior, or may be incapable of responding to pure tones on an audiometric test even though hearing acuity is normal. Other children with apparently normal hearing acuity may be so distracted by background sounds from the environment that normal speech comprehension is impossible in everyday situations. One of the most perplexing types of auditory disturbances is seen in the child who appears to have transient periods of auditory confusion during which he can understand only the simplest speech. These periods may occur several times a day or as seldom as once a week, and usually are not accompanied by any clinical signs of seizure activity.

Especially with children under the age of two, it is often difficult to distinguish between auditory behavior which is disturbed because of neurologic damage, and a delay in the development of auditory behavior as a consequence of mental retardation. In such cases it is often helpful to compare the way a child uses his hearing with the way he uses vision. A two-year-old who can localize quiet environmental sounds, but does not understand any words and gives no indication by facial expression or bodily activity that he recognizes familiar people or objects, may not be learning through vision to any greater extent than through hearing. But a child of the same age who likewise understands no speech, but spontaneously brings mother his boots and snowsuit when he sees brother and sister leaving for school, or picks up the telephone and carries on an animated conversation with the dial tone, is demonstrating conceptual activity based on visual learning, and it can be said that his use of vision is more like that of other two-year-olds than is his use of hearing.

As is true in other phases of the evaluation, the impressions gained from observing a child's receptive behavior must be interpreted in light of his mental growth, physical development, environmental background and emotional adjustment. Children with severe emotional disturbances may appear to be deaf; similarly, children raised from

infancy in an institution or in a home which provides little language stimulation may be slow to respond to spoken language or may have reduced understanding vocabularies. The techniques which have been mentioned are by no means adequate for the complete assessment of hearing acuity and use of hearing, but provide a means of identifying those children who should receive more thorough auditory testing.

Assessment of Concept Formation

Significant use of oral language implies ability to organize percepts into concepts. It is possible that some early elemental speech has little or no relation to conceptual functioning. One could never prove exactly what is taking place in a child's mind in speech learning, but from observation it seems possible that some approximations which parents accept as words are accidental babblings which bear relations to real words or ideas only in the adults' minds. The utterances could be fixed by parental rewards, and possibly the meanings of the words these sounds resemble are taught by the parents at a later date. Some words might also be produced on an echolalic level. On the other hand, at different times the same children might appear to have concepts they express by grunting and pointing before they have words for them, the concepts seeming to precede the oral symbols for expressing them. These speculations are purely academic and probably impossible to verify. The fact remains that useful speech depends upon having ideas. The reverse is not true. A child can have good concept formation and have no or relatively little oral language. An important part of the evaluation is to get some idea of the mental functioning and to see whether the expressive behavior is proportionate.

Fortunately ideation is indicated in other activities than speaking. One can, for instance, readily see the difference between the child who explores playthings fully and the one who merely pokes them and tries to put them up to his mouth. The examiner should have a variety of functional toys appropriate for various ages. Things that are realistic in terms of proportion, color and material are most useful. One can readily sympathize with a youngster who cannot see the similarity of some of the plastic horrors that are supposed to be pieces of miniature furniture and real furniture, but when he does not recognize and use miniatures which are very like the things in his environment, presumptions are raised. Miniature furniture, dishes, cutlery, pans, doll figures of family constellations, automobiles, tools, airplanes and trains can be used both in free play and cooperative play with the clinician, a parent or another child. A trained observer can readily see indications of understanding of uses, relations and imaginative play, and compare them with what the normal child of a like age would do.

The results of a psychologist's evaluation are important in this area, if the psychologist understands the child's handicap and how it will limit his performance. With many of the more involved cases the usual tests are inadequate, and one must rely upon a basic understanding of child development and language. The speech pathologist should be able to recognize whether or not the conceptual activity is adequate to support oral language, and be able to estimate the level of oral language that might be expected.

Examination of the Speech Musculature

Auditory disorders and symbolic language disturbances occur in many children as a result of damage to the central nervous system. Another common oral language handicap is slow, labored and indistinct speech due to muscle weakness or faulty control of the speech musculature. In ordinary conversation individual speech sounds are produced at the rate of approximately 10 per second, and the continuous production of speech sounds in words and phrases requires precise control and coordination of some 40 to 60 muscles in the trunk, neck, larynx, pharynx, tongue and face. Because of the speed and precision demanded of the speech musculature, motor impairment which might be so slight as to go unnoticed in a child's walking or hand movements may be a serious handicap to articulate speech.

It takes the average child six to seven years to perfect the perceptual and motor skills necessary for articulate speech. Nevertheless, many of the basic motor patterns which will be used in speaking can be observed in the sucking, swallowing, crying and breathing of the very young infant. Thus it is possible to gain an initial impression of the degree of motor dysfunction of the lips, tongue, muscles of mastication, velum, larynx, pharynx and muscles of breathing by studying the feeding, breathing and crying activities of infants under six months of age.

It is well known, for example, that the sucking reflex is absent or slow to appear in many brain-damaged infants. In some cases the reflex activity may be present but diminished, and the infant will have difficulty in sucking or swallowing due to weakness in the muscles of the face, tongue and pharynx. Such infants nurse slowly and seem to fatigue rapidly; usually much of the milk leaks out around the corners of the mouth. Excessive choking on milk or strained foods may be an indication of weakness in the pharyngeal and suprahyoid musculature. In rare instances early difficulty in swallowing is thought to be due to hyperactivity of the cricopharyngeus muscle, with consequent failure of this sphincter to relax to permit the passage of liquids into the esophagus. When such problems are detected early, corrective feeding techniques can be outlined for parents so that the infant can

eat more normally and at the same time develop the motor skills which will be necessary for speaking.

Voluntary control of the oral musculature begins to develop as the infant becomes skilled in eating solid foods. The lips, tongue and muscles of mastication are used selectively to manipulate the bolus and transport it to the back of the oral cavity for swallowing. As the infant gains skill in manipulating small bits of solids, many of the muscle movements used in eating begin to appear in his spontaneous vocal behavior. During the period of differentiated babbling, which usually appears by about six months, the infant begins to use lip and tongue movements in his syllable production, and in so doing is beginning to associate the tactile and kinesthetic sensations arising from movements of the articulators with the sounds produced by these movements. Considering the complexity of the perceptual tasks involved, it is remarkable that the average infant of 9 to 12 months has learned sufficient control of the speech musculature to imitate sounds, syllables and even words which he hears his parents speak.

Children with neuromotor involvement of the speech musculature often do not make the transition from the vegetative patterns of lip and tongue activity used in sucking and chewing to the more voluntary motor patterns used in speaking. In some children there may be reduced sensation in the lips and tongue so that motor learning is impaired. More often, however, weakness or paralysis in the lips, tongue, pharynx and muscles of mastication makes it necessary to continue feeding the child soft or strained foods which can be handled in the oral cavity by a sucking motion; consequently there is no reason for the child to develop specific tongue, lip and jaw activity. There are occasional instances in which a child seems unable to retain motor patterns for speech sound production, although the musculature is strong and well coordinated during eating. In these cases, which apparently are rare, the primary difficulty is not one of paralysis or muscle weakness, but a deficiency in motor learning and recall of motor patterns for speech.

Even though a movement such as elevating the tongue tip may appear during eating, a child cannot use this movement in speaking unless it is under voluntary control. The manner in which the speech musculature functions on a vegetative level thus serves to indicate the potential motor skills which may be trained for use in speaking. Through intensive muscle training it is often possible to improve the vegetative activities of the speech musculature and then to teach the child voluntary control of these movements for speech.

Complete examination of the speech musculature involves not only careful study of the vegetative and voluntary functions of specific muscle groups in the lips, tongue, cheeks, pharynx, larynx, neck and trunk, but also the extent to which the child has voluntary control of

motor patterns for breathing, phonation and articulation. The midline muscles of the speech mechanism do not show some of the characteristic symptoms of pyramidal and extrapyramidal damage that may be found in the arms and legs, and with the single exception of congenital spastic hemiplegia, in which the bilaterally innervated muscles of the speech mechanism are rarely affected, it is virtually impossible to anticipate the nature and extent of dysfunction of the speech musculature from a knowledge of the etiology and clinical classification of the child's condition. Motor dysfunction in speech is closely related to the over-all severity of the neuromotor handicap, but less to the clinical classification of pyramidal or extrapyramidal damage. Experience has shown that a program of muscle training for speech should be based on a child's specific neuromotor deficiencies rather than on the clinical classification of his symptoms. For this reason examination of the speech musculature is necessarily detailed, and must be carried out by a person thoroughly familiar with the neurophysiology of speech.

Summary of the Evaluation

It is important to remember that something useful should come from the evaluation for the parents, for other professional workers and especially for the child. Too often in involved cases reports reflect a coy modesty in which the clinician summarizes by writing that everything was inconclusive and that further testing must be done. Recognizing that going to the opposite extreme and making pronouncements that could have an unfortunate effect on a child's future on the basis of incomplete information is bad, the writers believe that the examiner should formulate some impression of what the problem appeared to be at that time, particularly when the evaluation is made at a doctor's request and the report is for him. Other professional persons should respect the "right to be wrong," and remember that when opinions differ, "someone" is wrong.

The clinician can summarize his impressions of how a child functioned in terms of the various components of oral language behavior, i.e. receiving sensory information, use of sensation, conceptual activity, symbol behavior, motor patterning of responses, and the efficiency of the execution of the motor activity. He can speculate about the interaction of these facets and factors which might explain poorer performance in any one of them. He can point out where deficits appeared to be greatest.

As an instance, when an athetoid performs the movements for words well enough so that a listener can recognize them by "lip reading" them, even though they cannot be understood from the sound alone, it would appear that the child has motor patterns for the words and

that his problem is in precise execution of those patterns. If he shows relatively good control of peripheral movements of the speech mechanism in eating and jargon, but does not organize them for words, even though use of hearing and tactile and kinesthetic sensation is good, one suspects an inability to organize and retain patterns for words. Even though such judgments are tenuous, they form the hypotheses on which experimental therapy can be based. Any diagnosis of a subtle language problem is apt to be tentative. Confirmation or negation often comes through the way a child responds to training.

All the observation and testing in the clinic must be integrated with the history in the summation. The history may indicate that the performance during the evaluation was not typical. It might suggest that behavior which could be interpreted as a difficulty in learning could be the result of lack of a suitable environment and handling in the home. Intelligent therapy should have a rational basis. The summation of the evaluation is the basis of the plan for training.

MANAGEMENT OF CHILDREN WITH COMMUNICATIVE DISORDERS

A detailed presentation of training techniques cannot be included in the present writing, nor would they be appropriate in it. An attempt is made, however, to propose answers to some of the questions which might come to the physician who has the responsibility for arranging programs for children. No "pat" answers can be offered for all children or all situations. The following may at least suggest points for consideration.

Which Children Should Be Referred for Training?

Too often the lack of speech or the use of substandard speech is automatically seen as a reason for initiating training. If a child's use of oral language is about as good as his over-all functioning, there is little point in training because no improvement can be expected. The fact of retardation should not preclude training. The educable retarded child can achieve acceptable articulation, although his rate of speech learning is slower than that of a normal child. There is no evidence that the trainable retarded child profits from formal training, but a favorable gorup environment will result in some gain in oral language among children whose opportunities have been limited. In any case the fact of poor performance alone should not dictate training. There should be some indication that performance could be better.

When the results of an evaluation are equivocal, a child is entitled to a reasonable trial period of training. Experimental training is often necessary to complete a diagnosis. In all cases parents' feelings must be

considered. Parents can often accept an unfavorable opinion better if at least some attempt has been made to work with a child.

When Should Training Be Started?

The answer to this question must be an individual one. With some cerebral-palsied children, for instance, it can be seen in the first few months that fundamental motor activities (breathing, phonation, eating, and so on) which will be modified later to be incorporated into speaking activity are not going to be adequate to support speech. Training can be initiated early so that physiologic readiness for speech can be improved by the time the child is ready to learn to talk. Delaying this training can be a serious hazard later because muscle imbalance may result in deformations of the thoracic cage and the maxillary arch which can result in much more difficulty with speech than the cerebral palsy itself could cause. Whenever there are threats to developing communicative skills which might be remediable, an attempt should be made to reduce or eliminate them even though actual speech learning would not normally have started at that time.

How Long Should Training Be Continued?

Children who have severe involvement can in many cases improve, but never achieve perfect or normal skill. When it appears that a fairly definite plateau has been reached, therapy should be terminated. It is not always wise to lose touch with them. If they are reviewed on at least a yearly basis, subsequent development may make further gains possible.

When it is likely that training may continue for a number of years, it is often well to have concentrated work for several months with free intervals between. Children can become bored with the constant drill, and the therapist and child can irritate each other. Intense periods of training can often accomplish more than the unbroken "cradle to grave" programs sometimes seen.

Can Parents and Other Persons Participate in the Training?

Ordinarily the assistance of other persons is welcomed by the speech therapist. There are children whose problems will respond to different management in the home, so that there will be better motivation and opportunity for communication. In these cases the therapist's time might be spent largely in counselling with parents and working with the child primarily to demonstrate procedures to the parent.

Professional time is at a premium, and few clinics can supply all the assistance most of the children need. Making use of parents, teachers and other workers is a way of greatly extending the learning opportunities for the children, and this is important.

Again the problem is individual. Some parents cannot gain sufficient insight. Some parents just do not work well with their children.

How Much Training Should Emphasize Speech Production?

Parents and other workers frequently see a communication problem as an inability to talk and can be restless if the therapist does not start to develop words immediately. Actually, the reason for the lack of speech is more important than the fact of the absence of speech. It is true that nothing is going to come out that does not first get in. This is true for audition, but equally true in connection with sensation used in motor learning. Among the most debilitating disorders are those which disrupt sensory input or the channeling and interpretation of sensation.

For the child with a hearing loss speech must often be amplified and other sensory channels utilized in supporting or substituting for hearing. When hearing is intact, but perception of sounds is disturbed, the auditory environment is organized so that learning can take place. The same principles apply in motor learning. Techniques of resistance and stimulation are used to get increased awareness of tactile and kinesthetic clues. Relaxation and other techniques for reduction of extraneous movement are applied to facilitate tactile and kinesthetic perceptual closure. The assumption is that conditions interfering with the development of communicative skills should be reduced before significant learning can take place.

What Training Should Therapists Have?

Specialization and advanced training are recognized in the medical profession, implying that not all members are equally equipped to render some services. The speech pathologist who works with children who have neurologic damage should also have advanced training and special experience. It is unlikely that a person without considerable graduate training, and not holding advanced certification in the American Speech and Hearing Association, would have the background to function in this area. At the same time mere possession of an advanced degree and level of certification would not guarantee competency in dealing with the problems, because the specialization and interests could have been in other directions. It is important to be sure that the personnel have adequate preparation to do the job.

Should Speech Be Taught to All Children?

Speech is a readily negotiable method of expression and the one most frequently used. Whenever it can be achieved, it is of course desirable. Nevertheless, the fact and degree of damage must be recognized. There are aphasic children whose expressive use of oral symbols is so limited, as well as others whose control of the speech mechanism is so poor, that little or no serviceable oral language is possible. Fortunately some of them have sufficient hand and arm function so that they can express themselves by pointing to letters and words printed on a board. Others whose arm function is limited have enough control of the head and neck so that they can grasp a pointer in the mouth and make use of such a board. In therapy an attempt should be made to exploit the most efficient manner of communication for each child. Insisting on a child's using speech can be frustrating and even limit his social effectiveness.

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THE HANDICAPPED CHILD

Programs and Resources

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The pediatrician encounters a substantial number of cases requiring nonmedical services to supplement medical treatment and to deal with social problems related to illness. The severely handicapped child or the child with a chronic condition requiring long-term care accounts for most such cases. The type of service needed may cover a wide range, including social, physical, educational, emotional, financial and recreational. The advice the pediatrician can give directly on such matters is limited, and he must depend on other resources in the community to deal with most of these needs. Failure to assist the parent in obtaining proper service may negate the treatment given by the physician or limit the degree of rehabilitation achieved.

The purpose of this article is to call attention to the services available in most larger communities and to indicate probable local sources of more specific information.

Phenomenal growth has characterized both public and voluntary agencies serving the handicapped in the past two decades. Rapid change in existing agencies, creation of new agencies, new services, and expanded public and voluntary programs have made it increasingly difficult to gain a clear understanding of what community resources are available to the physician working with the handicapped child and how he can make most effective use of them. It is hoped that in the following pages the functions of agencies providing these services and resources will be clarified.

In general, the resources listed will be available in many communities, although there is a wide variation among communities. The sources

of additional information as to what is available in a given community will be indicated.

As a guide to the agencies and organizations concerned with the care, treatment and education of the handicapped, the following listing may be useful to physicians. For the purposes of this paper, handicapping will include all types and all degrees of physical or mental conditions which impose long-term disability or educational limitations, such as orthopedic and neurologic conditions, serious defects of vision or hearing, speech disorders, epilepsy, diabetes, cardiac involvement, mental retardation or emotional disturbance.

In all communities the same kind of services in health, welfare and education which are available to the able-bodied are needed by the handicapped. So that he may utilize his abilities to the maximum degree, however, the handicapped child may require certain specialized services. When the involvement is severe, or when there are multiple handicaps, emotional problems or a mental deficit, requirements for special services are proportionately greater.

For the handicapped child one or more of a constellation of services may be needed, including hospitalization, nursing care, and surgery; physical and occupational therapy; speech and hearing therapy; psychological and psychiatric care; special education; social service; recreation; and vocational services. Other services sometimes needed are nursing, education and recreation for the home-bound child; fitting and training in use of artificial limbs and aids; brace making and fitting; provision of visual and hearing aids; institutional care; and parent and family education.

Services needed may be offered by tax-supported agencies and institutions, by voluntary, nonprofit organizations or in jointly operated programs. In this intricate maze of public and private agency functions those who need guidance or assistance are frequently unaware that services are available; also, agencies conducting programs may have difficulty reaching those who can benefit from the services they offer.

PUBLIC AGENCIES—FEDERAL, STATE, LOCAL

Governmental programs differ widely from state to state, varying in accordance with state laws, funds available and administrative procedures.

Crippled Children's Services

Established by the Social Security Act in 1935, this program of services for crippled children up to the age of 21 is administered jointly by the

Children's Bureau in the U.S. Department of Health, Education, and Welfare, and by state agencies. Through state appropriations matching federal grants, each state offers diagnostic services, medical care, hospitalization and surgery, and other selected services and care for children who are crippled or are suffering from conditions which lead to crippling. The statutory or administrative definition of crippling differs from one state to another. In some states services are limited to children with orthopedic handicaps and maxillofacial conditions, while in others a much larger group is served.

Demonstration projects have been operated under the Crippled Children's Services in cerebral palsy, rheumatic fever, epilepsy, hearing conservation, eye surgery, and others. Recent special programs have been developed in mental retardation and congenital heart disease. In most states the responsible agency is the state Department of Health, although, in a few, responsibility is placed with the state Department of Welfare, state university or a special commission. Eligibility for treatment service is based upon state standards of medical indigency. In some states the family assumes responsibility for as much of the cost of care as it is able to meet, while in others administrative regulations require the state agency to assume full responsibility. The Crippled Children's Services in the various states do not construct or operate any physical plants or institutions, but do purchase care from existing community medical and welfare facilities. Diagnostic clinics are held at specified times and places and recommendations made for treatment and follow-up when necessary. The professional staff of the state Crippled Children's Services carries through on these recommendations. The staff includes variously orthopedic nursing consultants, social workers, physical therapists, and others.

National Office: Crippled Children's Services; Children's Bureau; Social Security Administration, United States Department of Health, Education, and Welfare
Washington, D.C.

Vocational Rehabilitation

The basic program of vocational rehabilitation is a joint enterprise of the federal-state governments. The program serves adults primarily, and may be helpful in relation to older handicapped children for whom vocational plans are needed. There is an agency in each of the 50 states, Puerto Rico and the District of Columbia. The program is set up for the purpose of providing rehabilitation services to vocationally handicapped persons who are potentially employable. Each state furnishes a share of the total cost and administers its operating program under a

state plan which has been approved by the U.S. Office of Vocational Rehabilitation.

To be eligible for service a disabled person must satisfy the following conditions: (1) he must have a disability which presents a substantial handicap in securing employment; (2) he must be of working age or near it (16 years of age is the usual minimum, although legal working age is determined by the laws of the individual states); there must be a reasonable prospect that the disabled person will be employable when vocational rehabilitation services have been completed. Payment from public funds for services other than diagnostic, counseling, training, placement and follow-up is conditioned upon the economic circumstances of the disabled person.

Through the program, eligible disabled persons may secure any of the following services needed to restore function and enable them to secure suitable employment: diagnostic, medical, surgical and hospital services; artificial limbs and prosthetic appliances; counseling and guidance, education and job training; maintenance and transportation; tools, equipment; licenses; initial stocks of supplies and equipment when needed to give disabled persons a fair start in an occupation; placement in a job; and follow-up. Services ordinarily are purchased from hospitals, private physicians, schools, rehabilitation centers and other sources, except that counseling, guidance, placement and follow-up are furnished by state agency staff. In some states the vocational rehabilitation agency conducts an in-patient center offering rehabilitation services designed to restore maximum physical potential and offer vocational evaluation and retraining (e.g. Virginia, West Virginia, Pennsylvania, Oklahoma, Washington).

National Office: Office of Vocational Rehabilitation
Department of Health, Education, and Welfare
Miss Mary E. Switzer, Chief
Washington, D.C.

Aid to Dependent Children

Financial aid can be made available when necessary for care of children in situations in which one or both parents are dead, absent or incapacitated. This state-federal program provides funds for medical care as well as for other basic needs. Social casework services are available to these families and can be of assistance in working out social problems affecting the child. The local Department of Public Welfare administers this program.

National Office: Bureau of Public Assistance
Social Security Administration
Department of Health, Education, and Welfare
Washington, D.C.

War Orphans Education Program

Operated under the Veterans Administration, this program, established by Public Law 634, provides opportunities for "education to children whose education would otherwise be impeded or interrupted by reason of the death of a parent from a disease or injury incurred or aggravated in the Armed Forces." For children with physical or mental disabilities that would hamper regular education, the law provides for special training covering such areas as speech correction, lip reading, Braille reading and writing, one-hand typewriting, and personal adjustment.

Eligible also as dependent children are adopted children and stepchildren who are unmarried, legitimately born and under 21 years of age. In addition, children between 18 and 23 years of age of a deceased parent who served in World War I or II or in the Korean conflict may apply for the scholarships under this program.

National Office: Office of the Administrator of Veterans Affairs
Veterans Administration
Washington, D.C.

Special Services for Blind or Deaf Persons

Federal funds are available to cover the cost of books for day-school classes and schools for the blind. In recent years this provision has been extended to include Talking Books, Braille books, and maintenance and replacement of government-owned Talking Book machines. Braille and Talking Books are distributed postage-free to blind readers by 30 libraries throughout the country. Railroads, at their discretion, may carry a blind person and his guide for one full fare, as provided by an amendment to the Interstate Commerce Act. The same privilege has been extended by a number of bus lines.

Public Schools

In the larger metropolitan areas there are special schools for the handicapped or special classes in regular schools to provide services which make continued education possible. These include sight-saving equipment for the child with visual handicaps, and Braille lessons for those with severe sight loss or progressive conditions. For children with impaired hearing there may be lipreading instruction, speech therapy, and equipment to amplify sound. A growing service in the public schools is speech therapy for children with speech disorders (such as articulatory defects, cleft lip and palate, stuttering, speech disorders associated with cerebral palsy, language problems, and so on). For those with orthopedic or neuromuscular disabilities a special school staff will in-

clude physical therapists and occupational therapists. A few private residential institutions serve blind children exclusively.

A recent major emphasis in special education is on the mentally retarded. Those who are educable may be placed in special classes. Those who are not educable, but considered "trainable," are to an increasing extent receiving special school services which enable them to achieve social adjustment and secure training in performing self-care activities so that they will become less dependent upon others, and more easily cared for in their homes or the institutions in which they will live.

Institutional Care

Blind children of school age are most frequently educated in state residential schools, although many go to regular schools having a resource teacher or Braille class teacher available during the entire day or the services of an itinerant resource teacher at regular or needed intervals. Children suffering from deafness or severe hearing losses also frequently are referred to state residential schools, where for the most part the teaching of lipreading has replaced the older method of manual sign language. Information about these state services is available from the Department of Public Welfare, or the state Department of Institutions and Agencies.

Children with serious mental retardation are also eligible for state institutional care, although the age at which entrance is possible varies from state to state and frequently excludes the small child. Waiting lists frequently delay admissions. Emotionally disturbed children also may receive care in state tax-supported institutions, some of which provide for special units for treatment of emotional disorders.

State residential facilities for the care and treatment of children with orthopedic and neuromuscular disorders, including cerebral palsy, are found in some, but not all, states. Where they do exist, the inpatient population is generally small and, for the most part, subject to rather restricted admission policies. Most states provide for purchase of care in existing private institutions in selected instances, a procedure generally coming within the province of the state Crippled Children's Services program.

State hospitals for the chronically ill and tax-supported nursing home care do not offer a significant resource for the care of children, although, in cases of the severely disabled adolescent, placement may occasionally be made in such institutions.

Information about all state institutions is available from the state Department of Public Welfare or Department of Institutions and Agencies. A *Public Welfare Directory* (see Appendix) is published

annually which provides an up-to-date guide to all public health and welfare agencies in the several states.

Counties and municipalities covering large metropolitan areas may operate institutions for inpatient care of various types or have funds available to pay for such care in private institutions.

Private Residential Care

Information about private residential care for handicapped children is available from a number of sources. (See list of directories in Appendix.) A few private residential institutions serve small blind children exclusively, and others have services for the deafened. Private resources for speech rehabilitation are also available. Probably the most extensive private institutional programs, however, are those for the mentally deficient. A decrease has been noted in demand for residential care for the orthopedically handicapped child, and most institutions offering this type of service are operating at significantly less than capacity for children with such disabilities. This decrease may be ascribed in part to the lowered patient load of poliomyelitis patients and in part to the steadily increasing development of community resources to meet the needs of these children on an outpatient basis in their home communities.

Mental Health

Under the National Mental Health Act all states and territories now have community mental health programs. This includes operation or financial support of diagnostic, therapeutic and consultation services in existing health and welfare agencies, hospitals, schools and courts. Since these are chiefly in metropolitan areas, the provision of services in rural or sparsely populated areas presents continuing problems.

The National Mental Health Act is administered by the National Institute of Mental Health, which includes a Community Services Branch charged with the responsibility of assisting states to develop "effective methods of prevention, diagnosis and treatment of psychiatric disorders." In the individual states, however, there may be several official agencies having the primary function of treatment and care of the mentally ill. These are chiefly in the departments of public health, mental hygiene and public welfare.

In 14 states there are separate departments of mental health to administer the mental hospital program, while in others this program is administered within a variety of other agencies or departments.

National Office: Community Services Branch, National Institute of Mental Health, United States Public Health Service, Department of Health, Education, and Welfare
Washington, D.C.

VOLUNTARY AGENCIES

National health agencies reviewed here are those with substantial local service programs.

Although it is recognized that each of the following agencies has facets of program extending into research, professional training, public education, and other areas, limitations of space prevent discussion of more than their patient care program. The national headquarters office of these agencies is indicated, from which additional information about state and local resources may be obtained.

American Hearing Society

(919 - 18th Street, N.W., Washington 6, D.C.)

Through its 111 organizational affiliates the American Hearing Society carries out a program of prevention of deafness, conservation of hearing and rehabilitation of the hard of hearing. The affiliated units offer some or all of the following services: hearing testing; instruction in lipreading; auditory training; hearing aid consultation; speech correction; classes for preschool children; vocational guidance; and recreational programs for social adjustment.

Arthritis and Rheumatism Foundation

(10 Columbus Circle, New York 19, New York)

The main objectives of the Arthritis and Rheumatism Foundation and its 52 chapters throughout the United States are to discover, through research, the cause of and cure for arthritis and other rheumatic diseases and to provide improved treatment facilities for those afflicted with the diseases.

Patient-care services include arthritis clinics maintained through grants to hospitals and medical centers, and, in some localities, a home-care program which is carried out through mobile units. Approximately 40 per cent of the funds expended by local units of the Foundation are spent for direct patient care.

Goodwill Industries of America

(1913 N Street, Washington 6, D.C.)

Goodwill Industries operates a network of private rehabilitation workshops serving all types of handicapped persons. Services include job training, sheltered employment, vocational and personal counseling, job evaluation, recreation, religious guidance. Some Goodwill Industries also provide occupational or physical therapy services. Diagnostic

groups served are the blind, the deaf and hard of hearing, those with orthopedic and neurologic handicaps, and those with mental or emotional handicaps. There are 121 Goodwill workshops in 38 states.

Muscular Dystrophy Associations of America
(1790 Broadway, New York 19, New York)

The Muscular Dystrophy Associations have over 300 chapters organized in 48 states and in the District of Columbia. Although the chief aim of the Associations is research in muscular dystrophy and related diseases, the chapters operate or co-sponsor clinics in hospitals or medical centers in many states. All provide diagnostic and evaluation service and, in varying degrees, social service, physical therapy, occupational therapy, and vocational and recreational guidance. The chapters also assist in the purchase of wheelchairs, lifts, braces, and other orthopedic devices. Transportation may be provided, as needed, between schools, clinics and homes. One fourth of the funds raised is retained by local chapters for service programs in the community.

National Association for Retarded Children
(99 University Place, New York 3, New York)

The Association is represented by state and local affiliates in every state. In addition to public and professional education and support of research carried on through the national office, the local affiliates sponsor projects such as classes for trainable mentally retarded children, preschool programs, diagnostic and counseling services, and sheltered workshops in many communities. To an increasing extent they are initiating recreational facilities. Through the dissemination of information the Association has worked to develop an enlightened attitude toward the mentally retarded by the public.

The National Foundation
(800 - 2nd Avenue, New York 17, New York)

Formerly the National Foundation for Infantile Paralysis, the Foundation continues to carry research as the core of an expanded program to cover, in addition to the fields of poliomyelitis and virus diseases, investigations of disorders of the central nervous system, rheumatic diseases—including arthritis—and birth defects. The patient care program of the Foundation continues to be committed primarily to persons suffering from poliomyelitis. To this program will be added certain specific services to persons 18 years of age and under who suffer from arthritis or congenital abnormalities of the central nervous system.

National Multiple Sclerosis Society
(257 - 4th Avenue, New York 10, New York)

The National Multiple Sclerosis Society has local groups organized in all but two states. The Society seeks to stimulate, coordinate and support research directed toward determining the cause, prevention and cure of multiple sclerosis and related diseases of the central nervous system. Each of the local chapters conducts a patient aid program based upon community needs and within the limitations imposed by funds available. When opportunity presents and chapter funds are adequate, special clinics for multiple sclerosis are conducted within existing hospital facilities, providing diagnostic and evaluation services and patient management.

National Society for Crippled Children and Adults, Inc.
(2023 West Ogden Avenue, Chicago 12, Illinois)

Through the 1585 state and local affiliated units in 50 states, the District of Columbia and Puerto Rico, the National Society conducts a program of care and treatment, education and research. In direct services, over 1000 care and treatment facilities and services are operated or financed totally or partially by Easter Seal affiliates. Included are diagnostic and treatment centers, rehabilitation centers, inpatient centers, nursery schools, equipment loan pools, speech rehabilitation programs, resident and day camps, sheltered workshops, employment and therapy services for the homebound, and craft outlets. Additional services which may be offered are social service, employment placement, psychological services, recreation services, and provision of transportation, braces, appliances and equipment.

Parent education is fostered through organized parents' groups, training programs, and distribution of literature. The National Society library maintains a loan service for professional personnel and other interested persons, and publishes *Rehabilitation Literature*, a monthly journal.

Sister Elizabeth Kenny Foundation
(2400 Foshay Tower, Minneapolis 2, Minnesota)

Initiated to combat poliomyelitis by research, the Foundation's aim in patient care is now centered upon rehabilitation of persons with neuromuscular diseases and disorders. Disorders and disabilities for which treatment and rehabilitation are provided include poliomyelitis, nerve injuries, strokes, spinal injuries, congenital disabilities, cerebral palsy, spina bifida, birth injuries, amputations and prosthetic training, arthri-

tis, postfracture disabilities, muscular dystrophy, multiple sclerosis and contractures. The major facility operated by the Foundation is the Elizabeth Kenny Institute, a rehabilitation center located in Minneapolis. Other facilities operated by Foundation units are located in Detroit, Farmington (Michigan), Buffalo and Jersey City.

United Cerebral Palsy Associations, Inc.
(321 West 44th Street, New York 36, New York)

With affiliates in almost every state, the United Cerebral Palsy Associations stress research, public education and professional education in addition to a direct service program. The affiliates of the organization have organized diagnostic and treatment centers, nursery schools, recreation programs, sheltered workshops, vocational guidance and placement services for cerebral palsied persons. In addition, they purchase camperships and contribute financial assistance to existing treatment facilities in many communities throughout the United States. So far as possible, direct services are provided in cooperation with existing community facilities.

SOCIAL SERVICE WORK

The pediatrician frequently encounters situations in which the management of handicapping conditions is affected by involvement of the family or child in difficult problems of social or emotional conflict. In such instances the assistance of social service personnel can be of great value, since it can relieve the physician of time-consuming activities not directly related to medical care, but having a significant bearing upon the effectiveness of the medical program. Social workers are on the staffs of a large number of public and private agencies, but those which would be most directly concerned with the handicapped would be found through the following: community family health and welfare agencies, mental health clinics, social work staffs in hospitals and institutions, the state crippled children's services, the state division of child welfare. Some of the problems with which these skilled workers can help are unfavorable home conditions, family relationships, parent-child relationships, need for foster home placement, and institutionalization.

ADDITIONAL SOURCES OF INFORMATION

Community health and welfare agencies with programs for handicapped children also include such local agencies as community rehabilitation centers and treatment centers, visiting nurse associations, homemaking

services available to families in which the mother is disabled or absent because of illness, and related programs.

Additional sources of information about community services would be found among both public and private agency rosters, including the following:

State, County and City Health Departments

Public health nurses function as a liaison between the child, his family, and the community services and agencies. In performing these functions they gain an extensive background of information on community resources.

Community Welfare Councils

Variously termed as social planning councils, council of social agencies, and so on, the local welfare council is a clearing house of information about local health and welfare services. In the larger metropolitan centers the welfare council publishes a directory of agencies that is highly useful.

Community or State Health Council

The health council is an excellent source of information on agencies throughout a state or area, and on the personnel, functions and scope of program of the agencies in the health field in a given area.

University Hospitals and Medical Centers

Rich resources in diagnostic and clinic services, therapy and related functions are available through the various departments of universities, teaching hospitals and medical centers, both public and private. University centers, for instance, are the greatest single source of diagnostic service and therapy in speech rehabilitation and hearing conservation.

Meeting the needs of handicapped children and their families requires services from a wide range of public and private agencies in the fields of health, welfare, education, recreation and employment. The pediatrician who is alert to the services available from the various agencies can utilize to great advantage the program resources of one or of many agencies in planning a treatment program for an individual child. The serious inadequacies in what is presently available become apparent as one attempts to find a solution to certain problems such as long-term residential care of the severely disabled child who is mentally normal, the infant requiring custodial and full-time care for which

the family is unable to pay, a facility for education and vocational training of the adolescent requiring residential care, treatment facilities for the brain-injured; adequate diagnostic and therapy services in speech rehabilitation; adequate services in fitting children with artificial limbs and training them in their use; adequate services for the child with emotional disorders—to name only a few.

SUMMARY

There are given here the general resources in public and private agencies for care, treatment and education of handicapped children in the United States, and a list of directories of agencies serving the handicapped.

APPENDIX

Directories Listing Agencies Providing Services for the Handicapped

DIRECTORY OF FEDERAL AND PRIVATE AGENCIES WORKING WITH OR FOR THE HANDICAPPED IN THE UNITED STATES
(1959—104 p.) 25¢

Lists 59 agencies or organizations, with address and telephone number, name of executive, and purpose of the agency.

Available from: U. S. Committee for the Handicapped
Room 205
726 Jackson Place
Washington, D.C.

DIRECTORY OF STATE AND TERRITORIAL HEALTH AUTHORITIES
(1959—102 p.) (U.S. Public Health Service publ. no. 75, 1959 rev.) 35¢

Lists state agencies other than health departments designated to administer the grant program of the Children's Bureau for Crippled Children's Services, and state crippled children's programs under state departments of health.

Available from: U. S. Superintendent of Documents
Government Printing Office
Washington 25, D.C.

DIRECTORY FOR EXCEPTIONAL CHILDREN; EDUCATIONAL AND TRAINING FACILITIES
(1958—320 p., 3rd ed.) $6.00, clothbound

Lists and describes over 2000 schools, homes, clinics, hospitals and services for the socially maladjusted, mentally retarded, emotionally disturbed, orthopedically handicapped, cerebral palsied, speech handicapped, brain-injured, epileptic, cardiac, blind and deaf. It does not represent an accredited or an evaluated listing, however.

Available from: Porter Sargent, Publisher
11 Beacon Street
Boston 8, Massachusetts

DIRECTORY OF CATHOLIC FACILITIES FOR EXCEPTIONAL CHILDREN IN THE UNITED STATES
(1958—248 p., 3rd ed.) $2.75

Lists all residential and day schools now in operation under the Roman Catholic

school system in the United States for the education of the blind, deaf, hard of hearing, cerebral palsied, mentally retarded, partially seeing, the socially and emotionally maladjusted, and those requiring speech therapy, remedial reading lessons or child guidance. Gives information on purpose, capacity of school, class, or clinic, age requirements, and number on staff.

Available from: National Catholic Educational Association
1785 Massachusetts Avenue, N.W.
Washington 6, D.C.

DIRECTORY OF PUBLIC WELFARE
(1959—440 p.) $7.50

Covers programs, administrative practices and staff of national, state and local public welfare agencies in the United States and Canada.

Available from: American Public Welfare Association
1313 East 60th Street
Chicago 37, Illinois

DIRECTORY OF EDUCATION (U.S. Office of Education) 1958–59; PART I; FEDERAL GOVERNMENT AND STATES
(1959—76 p.) 45¢

Lists names of directors of special education by state. Directors of vocational rehabilitation and crippled children's services, in some states, are under the jurisdiction of the state department of education; in such instances their names are also listed.

Available from: U. S. Superintendent of Documents
Government Printing Office
Washington 25, D.C.

AMERICAN ANNALS OF THE DEAF
January issue (directory) $3.00

Contains listings of facilities for the deaf, including public residential schools, public day schools and classes, denominational and private schools in the United States, as well as a directory of schools and classes in Canada. Membership list of American Instructors of the Deaf and information on teacher training centers are also included.

Available from: Editor, American Annals of the Deaf
Gallaudet College
Washington 2, D.C.

DIRECTORY OF AGENCIES SERVING BLIND PERSONS IN THE UNITED STATES AND CANADA. Compiled by Wilma Saterlee
(1959—222 p.) $3.00

Available from: American Foundation for the Blind
15 West 16th Street
New York 11, New York

DIRECTORY OF THE AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, 1956; APPENDIX A: LISTINGS OF PUBLIC AND PRIVATE SCHOOLS AND HOMES FOR THE RETARDED
(127 p.) $1.00

Contains a listing of state, county, city and private homes and institutions for mentally retarded children in the United States. Publication in the list is not an endorsement of any school.

Available from: American Association on Mental Deficiency
P.O. Box 96
Willimantic, Connecticut

REHABILITATION CENTERS TODAY, by Henry Redkey.
(1959—231 p. Rehab. Service ser. no. 490) $1.00, paperbound. U. S. Office of Vocational Rehabilitation.

Contains reports on 77 rehabilitation centers, their operation, administration, policies and services, with a state-by-state directory.

Available from: U. S. Superintendent of Documents
Government Printing Office
Washington 25, D.C.

MEMBERSHIP DIRECTORY, AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION

Secretary, Dr. D. C. Spriestersbach, Department of Otolaryngology, University Hospital, Iowa City, Iowa.

DIRECTORY OF AMERICAN PSYCHOLOGICAL SERVICES
(1960—214 pp.) $1.50

American Board for Psychological Services, Inc.
Dr. Karl F. Heiser, President
Glendale, Ohio

DIRECTORY 1954–55, OUTPATIENT PSYCHIATRIC CLINICS AND OTHER MENTAL HEALTH RESOURCES IN THE UNITED STATES AND TERRITORIES
(1955—192 p.) $1.50

Contains listings of outpatient psychiatric clinics, state hospitals for mental disease, public institutions for mental defectives and epileptics, psychopathic hospitals, Veterans Administration hospitals, mental health associations, and state departments dealing with mental health.

Available from: National Association for Mental Health
10 Columbus Circle
New York 19, New York

RESIDENTIAL TREATMENT CENTERS FOR EMOTIONALLY DISTURBED CHILDREN: A LISTING
(1952—78 p.) 25¢. U. S. Children's Bureau

Listing does not constitute an endorsement, nor is there any evaluation of programs of the various centers. Descriptions and evaluations of the agencies' work are submitted by each agency.

Available from: U. S. Superintendent of Documents
Government Printing Office
Washington 25, D.C.

DIRECTORY OF VOCATIONAL COUNSELING AGENCIES
$1.50

Lists agencies currently approved by the Ethical Practices Committee of the National Vocational Guidance Association.

Available from: National Vocational Guidance Association
1605 New Hampshire Avenue, N.W.
Washington 9, D.C.

DIRECTORY OF COUNSELING AGENCIES
(56 p.) $1.00

Available from: American Personnel and Guidance Association
1605 New Hampshire Avenue, N.W.
Washington 9, D.C.

DIRECTORY OF NURSERY SCHOOLS AND CHILD CARE CENTERS IN THE UNITED STATES,
Compiled by Clark E. Moustakas and Minnie Berson.
(1951—171 p.) $1.50 Supplement (1953—88 p.) 50¢
(Not an approved or rated list of schools and centers; contains also lists of schools for exceptional children)

Available from: Merrill Palmer School
71 East Ferry Avenue
Detroit 2, Michigan

PRIVATE FOSTER CARE AGENCIES FOR CHILDREN
$2.00

Child Welfare League of America, Inc.
345 East 46th Street
New York 17, New York

RESOURCES FOR SPECIAL EDUCATION
Edited by Merle E. Frampton, Ph.D., and Elena D. Gall, Ed.D.
A list of official and voluntary agencies (1956), magazines and periodicals, directories, manuals and lists, with special listings of agencies, periodicals, books, pamphlets and articles for 22 specific areas of special education.

Porter Sargent, Publisher
11 Beacon Street
Boston 8, Massachusetts

DIRECTORY OF CAMPS FOR THE HANDICAPPED
Compiled by Eveline E. Jacobs
(1954) 50¢

Available from: National Society for Crippled Children and Adults, Inc.
2023 West Ogden Avenue
Chicago 12, Illinois

SHELTERED WORKSHOPS AND HOMEBOUND PROGRAMS—A DIRECTORY
National Association of Sheltered Workshops and Homebound Programs
$1.50

Available from: Howard G. Lytle, Treasurer
215 S. Senate Ave.
Indianapolis 25, Ind.

2023 W. Ogden Ave.
Chicago 12, Ill.

MANAGEMENT OF HEMIPLEGIC CHILDREN WITH PERIPHERAL SENSORY LOSS

MARGARET H. JONES, M.D.

Recently attention has been called to the frequency of peripheral sensory loss in brain-damaged children, especially those having hemiplegia. Management of such children, however, has continued to stress only motor training with the addition of bracing and surgery in case of orthopedic defects. Often, long periods of physical and occupational therapy have failed to develop functional use of the affected hand. In an adult, using multisensory stimulation rather than motor training, Forster has reported improved function in a hemiplegic patient whose deficit was mainly sensory. Whether emphasis on sensory stimulation in the management of the hemiplegic child with both sensory and motor deficits will lead to better functional use of the affected extremities is not known. Certainly, evaluation of both sensory and motor loss at as early an age as possible is important in understanding the child's total problem.

The purpose of this article is to present reported data on the types and frequency of peripheral sensory loss in hemiplegic children and to add hitherto unpublished material from our laboratory. Findings will be discussed in relation to the management of these children. A preliminary report on the use of multisensory stimulation in the training of the young child with peripheral sensory loss is included.

REPORTS IN THE LITERATURE OF TYPES AND FREQUENCY OF PERIPHERAL SENSORY LOSS

Tizard, Paine and Crothers,[12] Tachdjian and Minear[11] and Hohman, Baker and Reed[6] reported results of sensory testing in a total of 249

From the Department of Pediatrics, University of California at Los Angeles.

school-age and older cerebral-palsied children. Most were spastic hemiplegics, some triplegics or quadriplegics, with one side more involved than the other. Partial or complete sensory loss of one or more types ranged from 42 to 72 per cent, being 52 per cent for the group as a whole (Table 29).

The most frequently found deficits were stereognosis or form discrimination, two-point discrimination, and passive movement or position sense, in decreasing frequency in that order (Table 30).

Though partial or complete loss of light touch, pain, sharp-dull, hot-cold, wet-dry, occurred in many children, none of these latter modalities was defective unless one of the three most commonly impaired was also deficient.

Tachdjian and Minear[11] demonstrated an inverse ratio between the extent of sensory loss and the functional use of the extremity, as noted in Table 31. They found that 87.5 per cent of hemiplegics who had no use of the affected hand had sensory loss. Conversely, patients with normal use of the hand showed no sensory deficit.

Tizard, Paine and Crothers[12] reported strong correlation between skeletal undergrowth and sensory deficit (Table 32). Of 16 patients

TABLE 29. *Frequency of Sensory Loss*

NUMBER OF PATIENTS	SENSORY DEFICIT		AUTHOR
	Number	Per Cent	
106....	57	53.8	Tizard, Paine and Crothers[12]
47....	34	72.3	Hohman, Baker and Reed[6]
96....	40	41.7	Tachdjian and Minear[11]
Totals 249....	131	52.0	

TABLE 30. *Types of Sensory Loss (3 Most Frequent)*

TYPE	NUMBER			TOTAL	
	T.C.P.[12]	H.B.R.[6]	T.M.[11]	No.	%
Stereognosis or form discrimination.....	20	28	40	88	36
2-Point discrimination.....	14	23	31	68	28
Passive movement or position sense.....	15	14	16	45	20
Total number of patients in series.....	106	96	47	249	

TABLE 31. *Functional Use of the Hand versus Sensory Loss*[11]

FUNCTIONAL USE OF HAND	PER CENT HAVING SENSORY LOSS
None.....	87.5
Poor.....	68.9
Fair.....	30.0
Good.....	6.6
Normal.....	0.0

TABLE 32. *Skeletal Undergrowth versus Sensory Deficit*[12]

	TOTAL	SENSORY LOSS	HEMIANOPSIA
Skeletal undergrowth	16	14	14
No skeletal undergrowth	12	2	2

TABLE 33. *Severity of Sensory Deficit in Hemiplegia*[7]

Least severe	Face:	perioral
		lateral regions
	Trunk:	posterior
		anterior
	Leg:	upper
		lower
		foot
	Arm:	upper
		lower
Most severe	Hand	

showing skeletal undergrowth, 14 had sensory loss and also hemianopsia. Of 12 not showing skeletal undergrowth, only 2 showed sensory loss and hemianopsia.

Laine and Gros[7] discuss the degree of sensory loss in different parts of the affected side in hemiplegics, listing deficits in order of increasing severity (Table 33).

Laine and Gros report that the affected arm and leg may show improvement in physical function and in sensory perception after operation in which contralateral frontal, parietal, temporal and occipital lobes are removed en masse (hemispherectomy). They note that voluntary motion returned simultaneously with the return of position sense.

The reports presented above were obtained from tests of children of school age. In regard to the discriminatory abilities of normal young children, Haeusserman[4] has stated that children of 4½ years can differentiate familiar objects by tactile discrimination of form and texture. Monfraiz, Tardieu and Tardieu[9] report results with 12 geometric shapes used in the Grace Arthur Board with 218 children, ages 2½ to 8½ years. Those under 3½ failed to identify geometric shapes, but could recognize familiar objects. Children between 3½ and 6 could be graded by age by frequency of correct responses with the geometric shapes.

MATERIALS AND METHODS USED IN OUR STUDY*

Our study was undertaken to assess methods of testing sensory deficits,

* Assistance was given in these studies by Paul Greenberg in the summer of 1956, supported by the Spastic Children's League, and by L. Huhn in the summer of 1957, supported by a fellowship grant from the National Foundation. Some of these tests on adults were administered by occupational therapists at United Cerebral Palsy Association of Los Angeles County, in course of a research project supported by grant from United States Office of Vocational Rehabilitation.

TABLE 34. *Sensory Modalities Tested*

Exteroceptive	Light touch
	Sharp-dull
	Pain
	Hot-cold
	Wet-dry
Proprioceptive	Passive movement—position
	Pressure
	Vibration
Cortico-sensory	Rough-smooth
	Texture
	Weight-length
	Size (thickness)
	Shape (2 dimensions)
	Form (3 dimensions) (object discrimination)
	Tickle or scrape (probably a combination of modalities)

particularly cortical-sensory modalities, in the cerebral-palsied child under six years of age. For comparison 27 adults, 13 children from 6 to 12 years and 14 children under 6 years (10 between 3 and 6 and 4 from 19 months to 3 years) were tested. Most were spastic hemiplegics, a few quadriplegic, athetoid or mixed, with one side more involved than the other. Modalities studied were essentially those tested in Hohman's[5] series. They are listed in Table 34.

For children under 6 years of age a special table with glass insert was developed to allow the tester to view the child's extremities without either blindfolding him or expecting him to keep his eyes closed (Fig. 61). The child was held by an adult or seated in a suitable chair opposite the examiner.

In addition to the usual test objects, duplicates of those used for length, size, shape and form discrimination were made (Fig. 62). These were placed on top of the table and the child asked to pick out a matching object, rather than to answer verbally. Often several periods were required to secure satisfactory cooperation with the child between three and four years, but reproducible results were obtained in this group as well as those between four and six years.

For the child under three years of age, in our study, the only modalities that were tested satisfactorily were stereognosis—using small familiar objects (ball, key, safety pin, pencil) and checking to see whether the child could name them when presented visually before testing by tactile discrimination; light touch—feather, cotton or small object (penny, dowel or pencil) carefully placed in hand; response to pin prick—speed and type of response and localization on the affected side as compared to the good side.

McGraw[8] described response to pin pick in a series of 75 normal children, ages a few minutes to 4 years, as outlined in Table 35. She differentiated two major features in the behavior pattern to pin prick,

one the sensorimotor, the other the cognitive aspects. The sensorimotor was based on the response of application of the pin to the skin, the cognitive, to the pin as a visual stimulus. Only the sensorimotor was considered in our study, for the pin was kept out of sight.

The first phase of response was the newborn or diffuse phase, which consisted of diffuse bodily movement accompanied by crying and possibly local reflex withdrawal. The reaction was immediate.

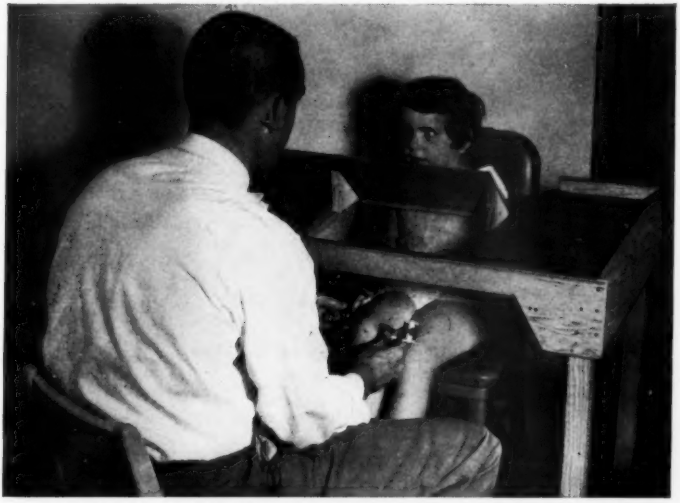

Fig. 61. Table with glass insert for testing sensory deficits in extremities.

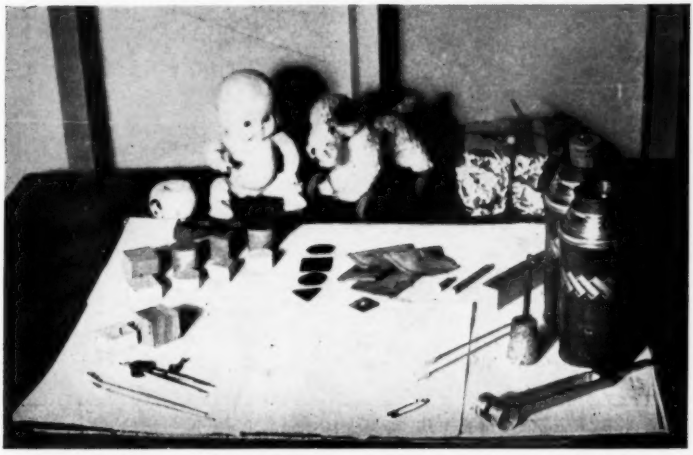

Fig. 62. Objects used for testing sensory deficits and form discrimination.

TABLE 35. *Response to Pin Prick*

RESPONSE	AGE OF CHILD
Newborn or diffuse phase	Minutes to 1 month
Inhibition of diffuse phase (cries only)	1 month to 3 months
General localization (deliberate withdrawal)	6-13 months
Specific localization	8 months on

Inhibition of this phase occurred after a month or so, the response being delayed diffuse body movement with less reflex withdrawal.

Later, about 6 months of age, the infant started to localize the area stimulated by deliberate withdrawal directed away from the source of irritation, as compared to reflex flexion type of withdrawal seen previously. Localization at this stage was mainly visual.

Specific localization began by about 8 months, as indicated by the child's ability to touch or rub the area stimulated. In McGraw's series of 75 normal infants the phase of specific localization had occurred in all before 500 days.

The affected side was regularly stimulated before the unaffected.

RESULTS OF EVALUATION (54 PATIENTS)

Our findings as to the type and incidence of sensory deficits in hemiplegic children from 6 to 12 years and in adults were similar to those of other investigators, especially Hohman et al.:[6] namely, that about three-fourths had demonstrable deficits, mainly of the cortico-sensory type. One or more of the three following modalities was either lost or less well perceived on the affected side—stereognosis or form discrimination, two-point discrimination, position or passive movement.

Comparing the results by age groups, it will be seen that those under six years of age showed approximately the same incidence of demonstrable cortico-sensory loss as did the older children and adults. In the children under three years of age the most frequent deficits demon-

TABLE 36. *Sensory Deficit by Age Group**

AGE	NUMBER OF PATIENTS	SENSORY DEFICIT	
		No.	%
Over 16 years	27	20	75
6-12 years	13	10	77
Under 6 years	14†	9	65
Total	54	39	74

* Los Angeles study: stereognosis or form, 2-point discrimination, position or passive movement.

† In 3 of the 14 patients, tests of this type were unsatisfactory.

strated were light touch, passive movement, abnormal response to pin prick.

Figure 63 indicates a breakdown of the findings into exteroceptive, proprioceptive and cortico-sensory types of sensory loss. Light touch, indicated by the number "1" on the left-hand series of graphs, was the most reproducible test in the very young child and could be applied satisfactorily to all. Without calling attention to the fact that the affected arm might be touched with cotton or a feather, 75 per cent of the group under 6 years of age failed to appreciate the stimulus. In children from 6 to 12, only 58 per cent failed to respond, and in the

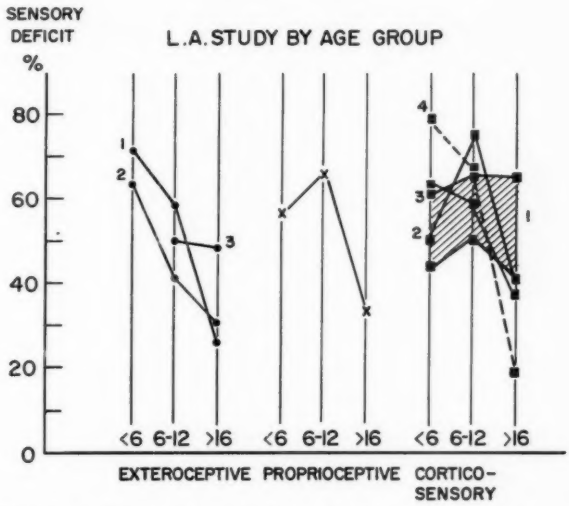

Fig. 63. Findings in exteroceptive, proprioceptive and cortico-sensory types of sensory loss.

adult, only 26 per cent. Good response occurred on the other side in all.

Similar findings were reported for pain or sharp-dull discrimination, indicated by number "2" on this same series of graphs. Number "3" on these graphs indicates the response to hot-cold stimulation, which was not satisfactory in many of the children under six, but showed no variation between older children and adults.

The middle graph indicates the result of tests for perception of passive movement or position sense, and this also appeared to improve with age.

On the right hand side of the chart the cortico-sensory loss, as noted by the shaded areas, representing loss of one or more of the fol-

lowing—form, shape, weight, length discrimination and object identification—remained at the same level in all ages. In this graph number "2" represents loss in two-point discrimination, number "3" loss in rough-smooth differentiation. The broken line "4" represents loss of localization to touch.

As in Tizard, Paine and Crothers's[12] series, no relation was found in our patients between intelligence, degree of atrophy of part, electroencephalographic abnormalities and incidence of sensory loss. We do not have data on length of the extremities.

COMMENTS

The findings outlined above support DeJong's[2] comment that "sensation and motion are interdependent and that severe motor disabilities may follow impairment of sensory functions."

For a discussion of the current concepts of the physiology of motor learning, the reader is referred to Hellebrandt's[5] review, which gives various hypotheses on the relation of sensory input to motor function, and Clark's[1] lecture on sensory experience and brain structure.

From the clinical point of view, Ogden, Robert and Carmichael's[10] report of children with congenital deficits in sensory perception, but without motor abnormality, who show a delay in sitting, standing and walking, suggests a possible relation of sensory loss to motor development. Forster's[3] success in the use of multisensory stimulation in retraining of an adult hemiplegic with a sensory loss due to cardiovascular accident is important in showing that, despite known central nervous system damage, improved sensory perception is possible with training and is followed by improved hand use. Current failures to achieve functional hand use with motor education alone in congenital or early acquired hemiplegics suggest the need of trial of another approach.

Evaluation of sensory perception, particularly of the cortico-sensory type, should be attempted even in young children before a therapy program is outlined. Re-evaluation of sensory modalities as the child matures and particularly before any surgical procedure is done is essential. As illustrated in case reports by Tizard, Crothers and Paine,[12] tendon transplant may be beneficial in patients with no sensory loss, but may not be helpful in those with sensory loss. These authors also found that the frequency of cortico-sensory loss is as great in the child whose hemiplegia was present from birth as in the patient who acquires the condition later, although the extent of involvement is usually greater in the latter children.

Hohman et al.[6] found that "very small areas of the hand might be involved leaving a major portion with good sensory perception." They

also stress the finding of impairment of perception, as for example the ability to differentiate two points at ½ inch on one side and 1½ inches on the other side. Sensations might be correctly, but more slowly, identified on the affected side as compared with the unaffected.

Again emphasizing the correlation between recovery of sensory perception and development of motor function, is Twitchell's[13] study in adults of return of finger reflexes which were deemed proprioceptive, as an index of final functional use of the hemiplegic hand. Without giving specific data, this author also states that "persistent defect of sensation of the affected limbs . . . particularly point localization, position sense, and other cortical discriminating functions is not conducive to good motor recovery."

PRELIMINARY RESULTS OF TRAINING INCORPORATING SENSORY STIMULATION

Recently studies have been begun in our laboratory aimed at determining the effect of multisensory stimulation in the young hemiplegic child. We are interested in the effects of such training, both on tested sensory deficit and on spontaneous motor function.

In the child under six years of age, sharply contrasting stimuli of temperature, texture, size and shape were presented first to the good hand and then the affected one. This was done in the form of a story told to the child, on an individual basis rather than in a group. Initial results are encouraging in that the frequency of spontaneous reach and grasp increased, first on the unaffected and then on the affected side. Graded series of motor performances were also constructed for which rewards were given. The child was shown what was wanted, but was not helped in achieving it. These tasks involve eye-hand coordination, beginning with a simple motion. Progression from simple to more difficult motor tasks was possible even at age 2½ years. In the older children, tactile discrimination with reward was set up, first calling attention to differences verbally by asking the child to feel and look at each of two disparate objects and finally to differentiate without vision. Gradually the children appeared to learn clues enough to make at least gross differentiations.

In the past the unaffected arm and hand were sometimes immobilized to force use of the affected side. This resulted in stuttering, increased seizures and behavior problems. It is true that in the above-outlined training the child is asked to use the affected side, but the other side is only gently restrained and for short periods. The tasks required of the affected side are carefully graded, beginning with simple ones in which success is easily attainable. Thus far, none of the undesirable side effects have been noted.

Training, using sensory stimulation, needs to be as carefully planned and carried out as does that for motor education. It needs to be done on an individual basis and by trained personnel and, as Forster notes, is time consuming. It needs to be combined with passive stretching if contractures are present.

SUMMARY

An essential part of the evaluation of the hemiplegic patient is the sensory examination. Sensory deficit is often associated with poor functional use of the hemiplegic hand.

It is possible, with some modifications of usual testing methods, to demonstrate sensory impairment or loss in children under six years of age. Table 37 reports major deficits found in the three age groups.

TABLE 37. *Major Sensory Deficits Demonstrated in Hemiplegic Children of Different Ages*

Over 6 years	Form or object discrimination
	2-Point discrimination
	Position sense—passive movement
3-6 years	Identification of small familiar objects by name
	Match shapes and forms ±
	Passive movement
Under 3 years	Perception of light touch (penny or dowel in hand)
	Response to pin prick (degree of localization)
	Passive movement

Our findings are similar to those of other authors in respect to frequency of sensory impairment, particularly cortico-sensory deficits (40 to 65 per cent). It is also of interest that deficits in light touch were three times as frequent (75 per cent) in children under 6 years of age as in adults (26 per cent).

Current studies of the effect of multisensory stimulation training on the development of motor function in young hemiplegic children are encouraging.

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